



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Meissner et al.

Serial Number: 09/393,023

Group Art Unit: 1646

Filed: September 9, 1999

Examiner: Kaufman, C.

For: Human Criptin Growth Factor

Attorney Docket: PF200D1

#26

PETITION UNDER 37 C.F.R. §§ 1.144 and 1.181(c)

RECEIVED

SEP 23 2002

TECH CENTER 1600/2900

John Doll
Director: Technology Group 1600
Washington, D.C. 20231

Sir:

Applicants hereby petition under 37 C.F.R. §§ 1.144 and 1.181(c) the restriction requirement (Paper No.23) mailed on June 19, 2002. Applicants submit concurrently herewith: a copy of the originally filed claims (Exhibit A); a copy of the first restriction requirement, Paper No.8 (Exhibit B); a copy of Applicants' provisional election with traverse and amendment (Exhibit C); a copy of the further restriction requirement, Paper No.12 (Exhibit D); a copy of Applicants' response to the further restriction requirement and provisional election with traverse (Exhibit E); a copy of the final restriction requirement, Paper No.17 (Exhibit F); a copy of the decision dated June 10, 2002 granting the petition filed on March 27, 2002 (Exhibit G); a copy of the subsequent restriction requirement, Paper No.23 mailed June 19, 2002 (Exhibit H); a copy of Applicants' provisional election with traverse of the restriction requirement of Paper No.23 (Exhibit I); a copy of part P-08 entitled, "Restriction Practice for Markush and Sequence Claims" from USPTO document, "The 21st Century Strategic Plan," released July 5, 2002 (Exhibit J); a copy of page 4 of the specification of the captioned application (Exhibit K); a copy of page 10 of the specification of the captioned application (Exhibit L); and a copy of the Federal Register: June 15, 1998, Vol. 63, No. 114, pages 32639-32644 (Exhibit M). No fee is believed due in connection with the filing of this petition, but in the event a fee is required, please charge the fees to our Deposit Account No. 08-3425.

I. Background

A. On September 9, 1999, Applicants filed the above-captioned application, which included claims 1-20. The originally submitted claims are shown in Exhibit A.

B. On December 13, 2000, a restriction requirement was mailed, Paper No.8 (Exhibit B), to Applicants indicating that restriction of the claims is required under 35 U.S.C. § 121 because the “inventions are distinct...and have acquired a separate status in the art.” *See* Paper No.8, page 4, third paragraph.

C. On May 17, 2001, Applicants submitted a provisional election with traverse and amendment under 37 C.F.R. § 1.143 (Exhibit C). In their response, Applicants traversed the restriction requirement under 37 C.F.R. § 1.143, giving reasons why the restriction was improper. In addition, Applicants provisionally elected the inventions of Group I, drawn to polypeptides (as set out by the Examiner in Paper No.8). Applicants also canceled claims 1-13, 15 and 17-18 and added new claims 21-95 directed to subject matter falling within the scope of Group I, as defined by the Examiner. For convenience, Applicants will refer to claims 21(a), 22, and the claims dependent therefrom, as “the full-length claims” and claims 21(b)-(k), 46(a)-(k), and 84, and the claims dependent therefrom, as “the fragment and variant claims.”

D. On July 6, 2001, the Examiner mailed Paper No.12 (Exhibit D). In Paper No.12, the Examiner acknowledged Applicants’ election with traverse of Group I (represented by claims 21-95). *See* Paper No.12, page 2, first paragraph. Upon reconsideration, the Examiner deemed the restriction between the groups proper. *See Id.* In addition, the Examiner required further restriction (i.e., a second restriction requirement) within the formerly presented Group I.

E. On September 5, 2001, Applicants submitted a response to the second restriction requirement imposed by the Examiner (Exhibit E). In their response, Applicants traversed the restriction requirement under 37 C.F.R. § 1.143, giving reasons why the restriction was improper, requested that the restriction be withdrawn, and provisionally elected claim 21(e) as required by 37 C.F.R. § 1.143. Applicants also reserved their right to petition. *See* Exhibit E, page 2, first full paragraph.

F. On November 26, 2001, the Examiner mailed Paper No.17 (Exhibit F). The Examiner acknowledged Applicants’ traversal (*see* Exhibit F, page 2, paragraph 2) and reconsidered the restriction requirement. After reconsidering the restriction requirement, the Examiner concluded that the “restriction is still deemed proper and is therefore made final.” *See* Exhibit F, page 2, paragraph 5.

G. Applicants petitioned the final requirement for restriction (Paper No.17) under 37 C.F.R. §§ 1.144 and 1.181(c) on March 27, 2002.

H. The petition was granted on June 10, 2002 (Paper No.22). In granting the petition, the Director of Technology Group 1600 stated that “it was determined that the

Groups as presented by the examiner were not entirely independent from each other or patentably distinct from each other.” *See* Exhibit G, page 2, last paragraph. Consequently, the restriction requirement and the Office Action of Paper No.17 were vacated and the application was forwarded to the Examiner for a new restriction.

I. On June 19, 2002, the Examiner mailed a new restriction requirement (Paper No. 23) arguing that Groups 1-27, as set out by the Examiner, were “independent.” *See* Exhibit H.

J. On September 19, 2002, Applicants submitted a provisional election with traverse under 37 C.F.R. § 1.143 (Exhibit I). In their response, Applicants traversed the new restriction requirement under 37 C.F.R. § 1.143, giving reasons why the restriction was improper. In addition, Applicants provisionally elected the inventions of Group 1, drawn to polypeptides (as set out by the Examiner in Paper No.23). Applicants also reserved their right to petition. *See* Exhibit I, page 2. The Director of Technology Group 1600 invited Applicants to submit the instant petition on the same day as the filing of the provisional election with traverse.

K. Applicants present the following reasons why the Examiner’s new restriction requirement is improper:

1. The Examiner failed to consider restriction of the invention as claimed and improperly created groups containing subject matter which differs from the subject matter of Applicants’ pending claims.
2. The Examiner failed to consider whether the claimed inventions were “distinct” as required by the plain and unambiguous meaning of the applicable statute, 35 U.S.C. § 121.
3. The claimed polypeptides are neither “independent” nor “distinct.”

II. The Examiner failed to consider restriction of the invention as claimed and improperly created groups containing subject matter which differs from the subject matter of Applicants' pending claims

Applicants respectfully point out that the Examiner failed to consider restriction of the invention as claimed and failed to group the inventions as claimed by Applicants, which is inconsistent with the restriction practice procedures set forth in the M.P.E.P. For example, M.P.E.P. § 808 reads as follows (emphasis in original):

Every requirement to restrict has two aspects: (A) the reasons (as distinguished from mere statement of conclusion) why the inventions *as claimed* are either independent or distinct; and (B) the reasons for insisting upon restriction therebetween as set forth in the following sections. M.P.E.P. § 808 at 800-47.

In addition, M.P.E.P. § 806.05(c) reads (emphasis added):

The inventions are distinct if it can be shown that a combination as claimed:

(A) does not require the particulars of the subcombination as claimed for patentability (to show novelty and unobviousness), and

(B) the subcombination can be shown to have utility either by itself or in other and different relations. M.P.E.P. § 806.05(c) at 800-42.

Further, M.P.E.P. § 808.02 reads (emphasis added):

Where, as disclosed in the application, the several inventions claimed are related, and such related inventions are not patentably distinct as claimed, restriction under 35 U.S.C. § 121 is never proper (MPEP § 806.05). M.P.E.P. § 808.02 at 800-48.

Moreover, M.P.E.P. § 814 reads (emphasis added):

The separate inventions should be identified by a grouping of the claims with a short description of the total extent of the invention claimed in each group, specify the type of relationship of each group as by stating the group is drawn to a process, or to a subcombination, or to product, etc. and should indicate the classification or separate status of each group, as for example, by class and subclass. M.P.E.P. § 814 at 800-56.

Therefore, the M.P.E.P. requires that the Examiner 1) consider the restriction of the inventions based on the invention as claimed and 2) group the alleged "separate inventions" in groups that contain subject matter of each pending claim, i.e., the subject matter as claimed.

In the instant case, the Examiner, in an effort to show independence of claimed subject matter (which is clearly dependent as disclosed in the application) and to avoid double patenting concerns, has created Groups 2-23 containing exclusionary language not

recited in the pending claims. For example, the Examiner created Groups 2-4 by adding the following italicized language to the claims (See Exhibit H (emphasis added)):

2. Isolated proteins comprising amino acid residues 1-173 of SEQ ID NO:2 *except for those proteins comprising amino acid residues 1-223 of SEQ ID NO:2.*
3. Isolated proteins comprising amino acid residues 24-223 of SEQ ID NO:2 *except for those proteins comprising amino acid residues 1-223 of SEQ ID NO:2.*
4. Isolated proteins comprising amino acid residues 24-67 of SEQ ID NO:2 *except for those proteins comprising amino acid residues 24-173 of SEQ ID NO:2, those proteins comprising amino acid residues 1-173 of SEQ ID NO:2, those proteins comprising amino acid residues 24-223 of SEQ ID NO:2, and those proteins comprising amino acid residues 1-223 of SEQ ID NO:2.*

Groups 5-23 also contain similar Examiner-created exclusionary language as emphasized above. By grouping the claims in this manner, the Examiner has added limitations not found in the pending claims. Since the Examiner did not consider the restriction of the inventions based on the invention as claimed and failed to group the alleged “separate inventions” in groups that contain subject matter of each pending claim, i.e., the subject matter as claimed, groups 2-23 are clearly improper.

III. The Examiner failed to consider whether the claimed inventions were “distinct” as required by the plain and unambiguous meaning of the applicable statute, 35 U.S.C.

§ 121

The Examiner has cited 35 U.S.C. § 121 as authority in requiring restriction of claims 21-95. See Exhibit H. Applicants contend that the Examiner improperly exercised her discretion in requiring restriction of the claimed inventions because the Examiner’s action is not consistent with the plain and unambiguous meaning of the applicable statute, 35 U.S.C. § 121. The first clause of 35 U.S.C. § 121 reads as follows (emphasis added):

If two or more independent and distinct inventions are claimed in one application, the Director may require the application to be restricted to one of the inventions.

The statute unambiguously requires that two or more inventions claimed in one application be both independent and distinct before the Director may exercise his discretion in requiring the application to be restricted to one of the inventions. Thus, the Examiner (acting under the Director) must satisfy a two-prong analysis before discretion requiring restriction may be invoked. First, the Examiner must conclude that the claimed inventions are “independent,”

and second, the Examiner must conclude that the inventions are “distinct.” It is clear from the statute that the term “independent” and the term “distinct” are not one in the same. As conceded in the M.P.E.P.:

‘Independent’, of course, means not dependent. If ‘distinct’ means the same thing, then its use in the statute and the rule is redundant. M.P.E.P. § 802.01 at 800-3.

In the instant case, the Examiner concluded that the claimed inventions are “independent” and consequently required restriction under 35 U.S.C. § 121 (*See* Exhibit H, page 4, in regard to Groups 1-23). Importantly, the Examiner did not determine whether the claimed inventions were “distinct.” In failing to do so, the Examiner improperly exercised her discretion because she did not first conclude that the inventions were both “independent and distinct,” as required by the statute.

Applicants acknowledge that the M.P.E.P. treats the statutory language of 35 U.S.C. § 121, “independent and distinct,” as “independent or distinct.” Specifically, M.P.E.P. § 803 reads as follows (emphasis added):

Under the statute an application may properly be required to be restricted to one of two or more claimed inventions if they are able to support separate patents and they are either independent (MPEP § 806.04- § 806.04(i)) or distinct (MPEP § 806.05- § 806.05(i)). M.P.E.P. § 803 at 800-3.

Thus, even though the statute unambiguously requires that two or more inventions claimed in one application be both independent and distinct before the Director may exercise his discretion and the M.P.E.P. recognizes that “independent” and “distinct” have two entirely different meanings (*see* M.P.E.P. § 802.01 discussed above), M.P.E.P. § 803 provides that Examiners may exercise their discretion to restrict the claimed inventions upon conclusion that claimed inventions are either independent or distinct. Thus, M.P.E.P. § 803 is inconsistent with the plain meaning of the statute.

In addition, M.P.E.P. § 803 is inconsistent with statements made in the recently released USPTO document entitled “The 21st Century Strategic Plan.” For example, in regard to restriction practice for Markush and sequence claims in Part P-08 (Exhibit J), the USPTO makes the following statement (emphasis added):

Current restriction practice under 37 C.F.R. § 1.142 needs to be clarified to specifically address restriction to a single independent and distinct invention.... “The 21st Century Strategic Plan,” Part P-08, July 5, 2002 (Exhibit J).

Further, M.P.E.P. § 803 is inconsistent with case law. For example, in *In re Weber*, 580 F.2d 455 (CCPA 1978), the court clearly stated that (emphasis added) “[i]t is apparent

that [35 U.S.C.] § 121 provides the Commissioner with the authority to promulgate rules designed to restrict an application to one of several claimed inventions when those inventions are found to be ‘independent and distinct.’ *Id.* at 459.

Moreover, Applicants respectfully point out that the Supreme Court, in *Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc.* 467 U.S. 837 (1984), has held that, where Congress has explicitly or implicitly left a gap for agencies to fill, the formulation of policy and the making of rules to fill any gap is within the power of the administrative agency, but where the intent of Congress is clear from the plain meaning of the statute, except for rare instances, “that it is the end of the matter.” *Id.* at 842. Congress, in enacting 35 U.S.C. § 121 with the phrase “independent and distinct,” has not left a gap (explicitly or implicitly) which empowers the USPTO to read the conjunction “and” as an “or” as is the case in M.P.E.P. § 803. Therefore, consistent with the statute, case law, and the USPTO’s official public commentary, and contrary to guidance given by M.P.E.P. § 803, an Examiner or any other person acting under the authority of the USPTO, may not exercise their discretion to restrict the claimed invention unless they first conclude that the claimed inventions are both “independent” and “distinct.”

IV. The claimed polypeptides are neither “independent” nor “distinct”

As stated above, 35 U.S.C. § 121 requires that two or more inventions claimed in one application be both independent and distinct before an Examiner may exercise her discretion in requiring restriction to one of the inventions. Applicants submit that, even in the event that the statute recited, “independent or distinct inventions,” rather than “independent and distinct inventions,” the Examiner’s restriction would remain improper because the claimed inventions are neither “independent” nor “distinct” as defined in M.P.E.P. § 802.01.

A. The claimed inventions are not independent

1. The Examiner improperly concluded that the claimed inventions are independent

Based on statements made by the Examiner in requiring restriction of the claimed invention, it is evident that the Examiner improperly concluded that the claimed inventions are independent. M.P.E.P. § 802.01 reads as follows (emphasis added):

The term ‘independent’ (i.e., not dependent) means that there is no disclosed relationship between the two or more subjects disclosed, that is, they are unconnected in design or effect.... M.P.E.P. § 802.01 at 800-3.

Further, M.P.E.P. § 808.01 reads as follows (emphasis added in part):

Where the inventions claimed are independent, i.e., where they are not connected in design, operation, or effect under the disclosure of the

particular application under consideration (MPEP § 806.04), *the facts relied on for this conclusion are in essence the reasons for insisting upon restriction.* This situation, except for species, is but rarely presented, since persons will seldom file an application containing disclosures of independent things. M.P.E.P. § 808.01 at 800-47.

Therefore, the inquiry in determining whether “inventions claimed are independent,” as set out in the M.P.E.P., requires the Examiner to consider whether the claimed invention is connected in design, operation, or effect under the disclosure of the particular application.

In determining that the inventions are independent, the Examiner states the following at page 4 of the restriction requirement (emphasis added):

Each of Groups 1-23 is directed to isolated proteins wherein the proteins of each Group differ in structure relative to the proteins of each of the other Groups. Because of the difference in structure between the isolated proteins of each of the Groups, they are not related to each other (i.e., they are independent) and would be expected to have different properties and characteristics from each other. *See* Exhibit H, page 4.

Therefore, the Examiner compared the structure of the polypeptides in one Examiner-created group relative to polypeptides in other Examiner-created groups. Since the Examiner did not consider the relatedness of the invention as disclosed in the instant application, as is required by the M.P.E.P., the Examiner’s conclusion that the claimed inventions are independent was improper.

Notwithstanding the above, Applicants contend that, under the disclosure of the captioned application, the polypeptides of the fragment and variant claims are clearly not “independent” from the polypeptides of the full-length claims. Applicants respectfully point out that the relationship between the polypeptides of the fragment and variant claims and the polypeptide of the full-length claims is explicitly disclosed in the captioned application. For example, as disclosed in the specification at page 4 (Exhibit K), line 26, the sequence of the polypeptide fragment of claim 21(f) is related to the full-length sequence of claim 21(a) in that the sequence of a fragment is contained within the full-length sequence. Likewise, the sequence of a variant polypeptide (e.g., of claim 46(a)) is related to the full-length sequence by virtue of containing a specified range of identical amino acids with respect to the full-length sequence. *See* page 10 of the specification (Exhibit L), lines 19-34. This analysis can similarly be applied to the remaining claims. Thus, under the disclosure of the captioned application, the claimed polypeptides have a structural relationship, connected in design, and, therefore, are “dependent” as defined in M.P.E.P. §§ 802.01 and 808.01.

2. The claimed inventions have a subcombination-combination relationship, thus they are not independent

The M.P.E.P. defines a combination as “an organization of which a subcombination or element is a part.” M.P.E.P. § 806.05(a) at 800-42. The USPTO has previously applied this subcombination-combination analysis to biological sequences. *See, e.g.,* Exhibit M, page 32640, third column, second full paragraph to page 32641, second paragraph. Here, the USPTO has characterized a large polynucleotide sequence as a combination and a fragment of the large sequence as a subcombination. Specifically, the USPTO states:

A claim such as ‘A gene comprising SEQ ID NO:1,’ can be viewed as a species claim in which the preamble recites a combination and the body of the claim recites a subcombination: The ‘gene’ is the combination and ‘SEQ ID NO:1’ (which is a fragment of the gene) is the subcombination....

Likewise, generic claims to sequences can be viewed as a genus of such combination-subcombination claims. For example, a claim such as ‘A nucleic acid comprising SEQ ID NO:1’ can be viewed as a genus claim in which each member of the genus (each species) is itself a combination-subcombination: Each member of the genus ‘nucleic acid’ is a combination containing the subcombination of ‘SEQ ID NO:1’ (which is a fragment of the nucleic acid). Federal Register, June 15, 1998, Volume 63, No. 114, page 32640, third column, last paragraph to page 32641, second paragraph.

Thus, as stated by the USPTO, fragments of a sequence are a subcombination of a larger sequence (combination). Following this analysis, claims to the full-length polypeptide sequence are claims to a combination and claims to fragments or variants of the full-length polypeptide sequence (i.e., the combination) are subcombination claims.

Further, based on the disclosure of the M.P.E.P., the USPTO views subcombination and combination claimed inventions as related (i.e., dependent). For example, M.P.E.P. § 802.01 states the following (emphasis added):

The term ‘independent’ as already pointed out, means not dependent. A large number of subjects between which, prior to the 1952 Act, division had been proper, are dependent subjects, such as, for example, combination and a subcombination thereof.... M.P.E.P. § 802.01 at 800-3.

In addition, M.P.E.P. subsection 806.05(a), titled “Combination and Subcombination or Element,” is found under M.P.E.P. § 806.05, titled “Related Inventions.” Therefore, since the claimed inventions have a subcombination-combination relationship and the PTO recognizes that subcombination and combination claims are related, i.e., dependent, claims to the full-length polypeptide sequence and claims to fragments or variants of the full-length are not independent.

Applicants submit that the subject matter of the full-length claims and the fragment and variant claims are not “distinct” as defined in M.P.E.P. § 802.01. M.P.E.P. § 802.01 reads as follows (emphasis in original):

The term ‘distinct’ means that two or more subjects as disclosed are related, for example, as combination and part (subcombination) thereof, process and apparatus for its practice, process and product made, etc., but are capable of separate manufacture, use, or sale as claimed, AND ARE PATENTABLE (novel and unobvious) OVER EACH OTHER (though they may each be unpatentable over the prior art). It will be noted that in this definition the term related is used as an alternative for dependent in referring to subjects other than independent subjects. M.P.E.P. § 802.01 at 800-3.

Thus, M.P.E.P. § 802.01 provides that two or more claimed subjects are “distinct” only when they are patentable over one another, i.e., they are two-way distinct.

As discussed above, the M.P.E.P. requires the Examiner to consider the restriction of the inventions based on the invention as claimed. Applicants respectfully point out that, if the polypeptide of the full-length claims was known in the art before the invention of the polypeptides of the fragment and variant claims, the fragment and variant claims would not be patentable as claimed. This is because the full-length sequence would anticipate the fragment and variant claims. Thus, claims 21-95 are not patentably distinct as defined by M.P.E.P. § 802.01.

V. Conclusion

In light of the above, the restriction requirement imposed by the Examiner in Paper No.23 (Exhibit H) was improper. First, the Examiner failed to consider restriction of the invention as claimed and instead improperly created groups containing subject matter which differs from the subject matter of Applicants' pending claims. Second, the Examiner failed to consider whether the claimed inventions were "distinct" as required by the plain and unambiguous meaning of the applicable statute, 35 U.S.C. § 121. Third, the separately claimed polypeptides are neither "independent" nor "distinct." Therefore, Applicants respectfully petition the Commissioner for the withdrawal of the restriction requirement. No fee is believed due in connection with the filing of this petition, but in the event a fee is required, please charge the fees to our Deposit Account No. 08-3425.

Respectfully submitted,

Dated: 19 Sept. 2002

Charles E. Van Horn
Charles E. Van Horn
Reg. No. 40,266

EXHIBIT

A



WHAT IS CLAIMED IS:

1. An isolated polynucleotide comprising a member selected from the group consisting of:
 - (a) a polynucleotide encoding the polypeptide comprising amino acid -23 to amino acid 207 as set forth in Figure 1;
 - (b) a polynucleotide encoding the polypeptide comprising amino acid 1 to amino acid 207 as set forth in Figure 1;
 - (c) a polynucleotide encoding the polypeptide comprising amino acid 1 to amino acid 150 as set forth in Figure 1;
 - (d) a polynucleotide encoding the polypeptide comprising amino acid 45 to amino acid 150 as set forth in Figure 1;
 - (e) a polynucleotide capable of hybridizing to and which is at least 70% identical to the polynucleotide of (a), (b), (c) or (d); and
 - (f) a polynucleotide fragment of the polynucleotide of (a), (b), (c), (d) or (e).
2. The polynucleotide of Claim 1 wherein the polynucleotide is DNA.
3. An isolated polynucleotide comprising a member selected from the group consisting of:
 - (a) a polynucleotide which encodes a mature polypeptide encoded by the DNA contained in ATCC Deposit No. 97142;
 - (b) a polynucleotide which encodes a polypeptide expressed by the DNA contained in ATCC Deposit No. 97142;
 - (c) a polynucleotide capable of hybridizing to and which is at least 70% identical to the polynucleotide of (a) or (b); and

(c) a polynucleotide fragment of the polynucleotide of (a), (b) or (c).

4. The polynucleotide of claim 2 comprising the sequence as set forth in Figure 1 from nucleotide 1 to nucleotide 771.

5. The polynucleotide of claim 2 comprising the sequence as set forth in Figure 1 from nucleotide 62 to nucleotide 771.

6. The polynucleotide of claim 2 comprising the sequence as set forth in Figure 1 from nucleotide 151 to nucleotide 771.

7. The polynucleotide of claim 2 comprising the sequence as set forth in Figure 1 from nucleotide 283 to nucleotide 600.

8. A vector containing the DNA of Claim 2.

9. A host cell genetically engineered with the vector of Claim 8.

10. A process for producing a polypeptide comprising: expressing from the host cell of Claim 9 the polypeptide encoded by said DNA.

a 11. A process for producing cells capable of expressing polypeptide comprising genetically engineering cells with the vector of Claim 8.

12. A polypeptide comprising a member selected from the group consisting of (i) a polypeptide having the deduced amino acid sequence of Figure 1 and fragments,

analog and derivatives thereof; and (ii) a polypeptide encoded by the cDNA of ATCC Deposit No. 97142 and fragments, analogs and derivatives of said polypeptide.

13. A compound which activates a receptor for the polypeptide of claim 12.

14. A compound which inhibits the the polypeptide of claim 12.

15. An antibody against the polypeptide of claim 12.

16. A process for identifying compounds which inhibit activation of the polypeptide of claim 12 comprising:

contacting cells which express a CGF receptor on the surface thereof with labeled CGF and a compound to be screened under conditions suitable for binding of ligands to said receptor; and

determining the extent of binding of labeled CGF to the receptor by measuring the amount of label attached to the receptor.

17. A process for identifying compounds which inhibit activation of the polypeptide of claim 12 comprising:

contacting cells which express a CGF receptor on the surface thereof with a compound to be screened under conditions suitable for binding of ligands to said receptor; and

determining the extent of binding of of the compound to the receptor and the lack of a signal generated by the binding.

18. A process for identifying compounds which activate a receptor to the polypeptide of claim 12 comprising:

contacting cells which express a CGF receptor on the surface thereof with a compound to be screened under conditions suitable for binding of ligands to said receptor; and

determining the extent of binding of the compound to the receptor and the presence of a signal generated by the binding.

19. A process for diagnosing a disease or a susceptibility to a disease related to a mutation in the polynucleotide of claim 1 comprising:

determining a mutation in the polynucleotide of claim 1.

20. A diagnostic process comprising:

analyzing for the presence of the polypeptide of claim 12 in a sample derived from a host.

EXHIBIT

B



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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09/393,023 09/09/99 MEISSNER F PF-200

HM22/1213

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KAUFMAN, C

ART UNIT

PAPER NUMBER

1646

12/13/00



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DATE MAILED:

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HGS PATENT DEPT

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/393,023

Applicant(s)

MEISSNER ET AL.

Examiner

Claire M. Kaufman

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 September 1999.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claims 1-20 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-13, drawn to polynucleotide, vector, host cell, method of producing modified cell, method of producing polypeptide, polypeptide, and agonist, classified in Class 435, subclasses 69.1.
- II. Claim 14 and 15, drawn to antagonist and antibody, classified in Class 530, subclass 388.24.
- III. Claims 16-18, drawn to process for identifying agonist or antagonist with binding assay, classified in Class 435, subclass 7.21.
- IV. Claim 19, drawn to method of diagnosing by mutation analysis, classified in Class 435, subclass 6.
- V. Claim 20, drawn to method of detecting polypeptide presence, classified in Class 435, subclass 7.1, for example (classification dependent on method steps).

The inventions are distinct, each from the other because of the following reasons:

The protein of Group I is related to the antibody of Group II by virtue of being the cognate antigen, necessary for the production of the antibodies. Although the protein and antibody are related due to the necessary steric complementarity of the two, they are distinct inventions because the protein can be used for another and materially different process other than for production of the antibody, such as to assay or purify the natural receptor for the protein or in assays for the identification of agonist or antagonists of the receptor protein. The methods of Group I are unrelated to the antibody of Group II because the antibody is not required for the methods and can be used in a materially different process such as immunoprecipitation. The nucleic acid encodes the protein, but cannot itself be used to make the antibody or antagonist. The protein is related to the antagonist because they interact, however, they are necessarily structurally and functionally distinct.

Groups I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product

as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the protein of Group I which is required for the assays of Group III can be used for a materially different process such as in performing as an antigen in the making of an antibody or in isolation of its native receptor. Additionally, the methods of Group I are distinct from those of Group III because they have materially different steps and purposes/endpoints. The nucleic acid cannot be used in the methods of Group III.

The nucleic acid of Group I and method of Group IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the nucleic acid of Group I can be used for a materially different process such as for screening a cDNA library to isolate species homologues or to produce the encoded protein. The methods of Groups I and IV are distinct because they are unrelated in process steps and function/use.

The products of Group I are unrelated to the method of Group V in that the agonist or nucleic acid of Group I is not required for the detection of the protein in a sample from a host. This process maybe practiced with antibodies to the protein. Additionally, the agonist or nucleic acid may be used for materially different processes such as agonist activation of the receptor or nucleic acid blotting (*e.g.*, Southern blotting). The methods of Groups I and V are distinct because the methods of Group I do not require components that can be used in that of Group V (*e.g.* antibodies or sample from host). They also have materially different process steps.

Group II is unrelated to and distinct from Groups III and IV. The antibody of Group II is not required for the processes of Groups III and IV. Additionally the antibody may be used for materially different processes such as for immunoaffinity purification of its antigen or for immunocytochemistry to identify protein presence in specific tissues.

The products of Groups II and processes of Group V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the antibody of Group II may be

used for another materially different process such as to purify the polypeptide. Additionally, the process of Group V can be practiced with another materially different product, such as with its native receptor.

Groups III-V are unrelated processes that are functionally distinct and may be practiced in different manners, and if determined to be patentable, would also be patentably distinct with one not required for the other. The process for identifying agonists and antagonist of Group III does not require either DNA or antibodies, but does require the CGF receptor. The method of Group IV for diagnosing through mutation analysis requires polynucleotides but not antibodies or the receptor. The method of Group V of detecting polypeptide presence from a cell sample can be practiced with the antibody but not DNA, nor does it require that the receptor be present.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and the search required for one group is not coextensive with any other, restriction for examination purposes as indicated is proper.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Application/Control Number: 09/393,023

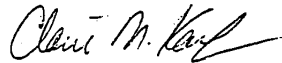
Page 5

Art Unit: 1646

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. Please advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.



Patent Examiner, Art Unit 1646

December 12, 2000

EXHIBIT

C



VIA HAND DELIVERY MAY 17, 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Meissner et al.

Application Number: 09/393,023

Group Art Unit: 1646

Filed: September 9, 1999

Examiner: Kaufman, C.

Title: Human Criptin Growth Factor

Attny. Docket No.: PF200D1

PROVISIONAL ELECTION UNDER 37 C.F.R. § 1.143
WITH TRAVERSE AND AMENDMENT UNDER 37 C.F.R. § 1.111

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SEP 23 2002
TECH CENTER 1600/2900

Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action dated December 13, 2000, Applicants provisionally elect, *with traverse*, Group I represented by newly added claims 21 to 95, for further prosecution. Applicants reserve the right to file one or more divisional applications directed to the non-elected inventions should the restriction requirement be made final. Applicants submit concurrently herewith: (a) a Supplemental Information Disclosure Statement, Form PTO/SB/08, and copies of references AG to AK; (b) a Petition for an Extension of Time for five (5) months, up to and including May 17, 2001; (c) a Fee Transmittal Sheet; and (d) a copy of the Second Preliminary Amendment submitted on December 8, 1999 and the returned date stamped postcard. Please amend the application as follows.

Amendments

In the Specification:

On page 1, please delete the first paragraph after the title, which begins "This application is a Divisional . . ." and replace it with:

-- This application is a Divisional of U.S. Application No. 08/471,371 filed June 6, 1995, now U.S. Patent 5,981,215 issued November 9, 1999.--

Please delete the fourth paragraph on page 4, which begins "A polynucleotide encoding a polypeptide of the present invention . . ." and ends " . . .has conserved cysteine residues in common with cripto growth factor," and replace it with:

--A polynucleotide encoding a polypeptide of the present invention was discovered in a cDNA library derived from human pancreatic cancer tissue. It is structurally related to the human cripto growth factor. It contains an open reading frame encoding a protein of 223 amino acid residues of which approximately the first 23 amino acids residues are the putative leader sequence such that the mature protein comprises 200 amino acids. As shown in figure 2 the polypeptide of the present invention has conserved cysteine residues in common with cripto growth factor.--

In the Claims:

Please cancel claims 1-13, 15, and 17-18 without prejudice.

Please add the following new claims:

--21. (New) An isolated protein comprising a polypeptide having an amino acid sequence selected from the group consisting of:

- (a) amino acid residues 1 to 223 of SEQ ID NO:2;
- (b) amino acid residues 1 to 173 of SEQ ID NO:2;
- (c) amino acid residues 24 to 223 of SEQ ID NO:2;
- (d) amino acid residues 24 to 67 of SEQ ID NO:2;
- (e) amino acid residues 24 to 173 of SEQ ID NO:2;
- (f) amino acid residues 45 to 128 of SEQ ID NO:2;
- (g) amino acid residues 68 to 173 of SEQ ID NO:2;
- (h) amino acid residues 68 to 223 of SEQ ID NO:2;
- (i) amino acid residues 129 to 207 of SEQ ID NO:2;
- (j) amino acid residues 174 to 223 of SEQ ID NO:2; and
- (k) a polypeptide fragment of amino acids 1 to 223 of SEQ ID NO:2 wherein said polypeptide fragment stimulates cell growth.

22. (New) An isolated protein of claim 21 which comprises amino acid residues 1 to 223 of SEQ ID NO:2.

23. (New) The isolated protein of claim 21 which comprises amino acid residues 1 to 173 of SEQ ID NO:2.

24. (New) The isolated protein of claim 21 which comprises amino acid residues 24 to 223 of SEQ ID NO:2.

25. (New) The isolated protein of claim 21 which comprises amino acid residues 24 to 67 of SEQ ID NO:2.

26. (New) The isolated protein of claim 21 which comprises amino acid residues 24 to 173 of SEQ ID NO:2.

27. (New) The isolated protein of claim 21 which comprises amino acid residues 45 to 128 of SEQ ID NO:2.

28. (New) The isolated protein of claim 21 which comprises amino acid residues 68 to 173 of SEQ ID NO:2.

29. (New) The isolated protein of claim 21 which comprises amino acid residues 68 to 223 of SEQ ID NO:2.

30. (New) The isolated protein of claim 21 which comprises amino acid residues 129 to 207 of SEQ ID NO:2.

31. (New) The isolated protein of claim 21 which comprises amino acid residues 173 to 223 of SEQ ID NO:2.

32. (New) The isolated protein of claim 21 which comprises a polypeptide fragment of amino acids 1 to 223 of SEQ ID NO:2 wherein said polypeptide fragment stimulates cell growth.

33. (New) The isolated protein of claim 21 wherein the amino acid sequence further comprises a heterologous polypeptide.

34. (New) The isolated protein of claim 24, wherein the amino acid sequence further comprises a heterologous polypeptide.

35. (New) The protein of claim 21, wherein said isolated protein is glycosylated.

36. (New) A composition comprising the isolated protein of claim 21 and a pharmaceutically acceptable carrier.

37. (New) A protein produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the isolated protein of claim 21; and

(b) recovering the protein.

38. (New) An isolated protein comprising an amino acid sequence selected from the group consisting of:

(a) the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142;

(b) the mature form of the polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142; and

(c) a polypeptide fragment of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142 wherein said polypeptide fragment stimulates cell growth.

39. (New) The protein of claim 38 which comprises the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142.

40. (New) The protein of claim 38 which comprises the mature form of the polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142.

41. (New) The protein of claim 38 which comprises a polypeptide fragment of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142 wherein said polypeptide fragment stimulates cell growth.

42. (New) The isolated protein of claim 38 wherein the amino acid sequence further comprises a heterologous polypeptide.

43. (New) The isolated protein of claim 38, wherein said protein is glycosylated.

44. (New) A composition comprising the protein of claim 38 and a pharmaceutically acceptable carrier.

45. (New) A protein produced by a method comprising:

- (a) culturing a host cell under conditions suitable to produce the protein of claim 38; and
- (b) recovering the protein.

46. (New) An isolated protein comprising an amino acid sequence 90% or more identical to an amino acid sequence selected from the group consisting of:

- (a) amino acid residues 1 to 223 of SEQ ID NO:2;
- (b) amino acid residues 1 to 173 of SEQ ID NO:2;
- (c) amino acid residues 24 to 223 of SEQ ID NO:2;
- (d) amino acid residues 24 to 67 of SEQ ID NO:2;
- (e) amino acid residues 24 to 173 of SEQ ID NO:2;
- (f) amino acid residues 45 to 128 of SEQ ID NO:2;
- (g) amino acid residues 68 to 173 of SEQ ID NO:2;
- (h) amino acid residues 68 to 223 of SEQ ID NO:2;
- (i) amino acid residues 129 to 207 of SEQ ID NO:2;
- (j) amino acid residues 173 to 223 of SEQ ID NO:2; and
- (k) a polypeptide fragment of amino acids 1 to 223 of SEQ ID NO:2 wherein said polypeptide fragment stimulates cell growth.

47. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 1 to 223 of SEQ ID NO:2.

48. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 1 to 173 of SEQ ID NO:2.

49. (New) The isolated polypeptide of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 24 to 223 of SEQ ID NO:2.

50. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 24 to 67 of SEQ ID NO:2.

51. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 24 to 173 of SEQ ID NO:2.

52. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 45 to 128 of SEQ ID NO:2.

53. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 68 to 173 of SEQ ID NO:2.

54. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 68 to 223 of SEQ ID NO:2.

55. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 129 to 207 of SEQ ID NO:2.

56. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to amino acid residues 173 to 223 of SEQ ID NO:2.

57. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 90% or more identical to a polypeptide fragment of amino acids 1 to 223 of SEQ ID NO:2 wherein said polypeptide fragment stimulates cell growth.

58. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 1 to 223 of SEQ ID NO:2.

59. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 1 to 173 of SEQ ID NO:2.

60. (New) The isolated polypeptide of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 24 to 223 of SEQ ID NO:2.

61. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 24 to 67 of SEQ ID NO:2.

62. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 24 to 173 of SEQ ID NO:2.

63. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 45 to 128 of SEQ ID NO:2.

64. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 68 to 173 of SEQ ID NO:2.

65. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 68 to 223 of SEQ ID NO:2.

66. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 129 to 207 of SEQ ID NO:2.

67. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to amino acid residues 173 to 223 of SEQ ID NO:2.

68. (New) The isolated protein of claim 46 which further comprises an amino acid sequence 95% or more identical to a polypeptide fragment of amino acids 1 to 223 of SEQ ID NO:2 wherein said polypeptide fragment stimulates cell growth.

69. (New) The isolated protein of claim 46 wherein the amino acid sequence further comprises a heterologous polypeptide.

70. (New) The isolated protein of claim 46, wherein said isolated protein is glycosylated.

71. (New) A composition comprising the isolated protein of claim 46 and a pharmaceutically acceptable carrier.

72. (New) A protein produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the protein of claim 46; and

(b) recovering the protein.

73. (New) An isolated protein comprising an amino acid sequence 90% or more identical to an amino acid sequence selected from the group consisting of:

(a) the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142;

(b) the mature form of the polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142; and

(c) a polypeptide fragment of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142 wherein said polypeptide fragment stimulates cell growth.

74. (New) The isolated protein of claim 73 which further comprises an amino acid sequence 90% or more identical to the amino acid sequence of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142.

75. (New) The isolated protein of claim 73 which further comprises an amino acid sequence 90% or more identical to the amino acid sequence of the mature form of the polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142.

76. (New) The isolated protein of claim 73 which further comprises an amino acid sequence 90% or more identical to the amino acid sequence of a polypeptide fragment of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142 wherein said polypeptide fragment stimulates cell growth.

77. (New) The isolated protein of claim 73 which further comprises an amino acid sequence 95% or more identical to the amino acid sequence of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142.

78. (New) The isolated protein of claim 73 which further comprises an amino acid sequence 95% or more identical to the amino acid sequence of the mature form of the polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142.

79. (New) The isolated protein of claim 73 which further comprises an amino acid sequence 95% or more identical to the amino acid sequence of a polypeptide fragment of the complete polypeptide encoded by the cDNA clone contained in ATCC Deposit No. 97142 wherein said polypeptide fragment stimulates cell growth.

80. (New) The isolated protein of claim 73 wherein the amino acid sequence further comprises a heterologous polypeptide.

81. (New) The isolated protein of claim 73 wherein said isolated protein is glycosylated.

82. (New) A composition comprising the isolated protein of claim 73 and a pharmaceutically acceptable carrier.

83. (New) A protein produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the isolated

protein of claim 73; and

(b) recovering the protein.

84. (New) An isolated protein comprising at least 30 contiguous amino acids of SEQ ID NO:2.

85. (New) The isolated protein of claim 84 further comprising at least 50 contiguous amino acids of SEQ ID NO:2.

86. (New) The isolated protein of claim 84 wherein the amino acid sequence further comprises a heterologous polypeptide.

87. (New) The isolated protein of claim 84 wherein said isolated protein is glycosylated.

88. (New) A composition comprising the isolated protein of claim 84 and a pharmaceutically acceptable carrier.

89. (New) A protein produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the isolated protein of claim 84; and

(b) recovering the protein.

90. (New) An isolated protein comprising at least 30 contiguous amino acids of the polypeptide encoded by the cDNA contained in ATCC Deposit No. 97142.

91. (New) The isolated protein of claim 90 further comprising at least 50 contiguous amino acids of the polypeptide encoded by the cDNA contained in ATCC Deposit No. 97142.

92. (New) The isolated protein of claim 90 wherein the amino acid sequence further comprises a heterologous polypeptide.

93. (New) The isolated protein of claim 90 wherein said isolated protein is glycosylated.

94. (New) A composition comprising the isolated protein of claim 90 and a pharmaceutically acceptable carrier.

95. (New) A protein produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the isolated protein of claim 90; and

(b) recovering the protein.--

Remarks

Claims 14, 16, 19-20 and new claims 21-95 are pending in the instant application.

Claims 1-13, 15, and 17-18 have been canceled, and new claims 21 to 95 have been added to more particularly point out and distinctly claim the subject matter Applicants regard as the invention. Support for the newly added claims is found throughout the specification as filed. Particularly, support for claims 21-32 and 38-41 can be found, for example, at page 4, lines 9-28; page 18, lines 18-31; page 43, original claim 1 and 3; and Figure 1. Support for claims 33-34, 42, 69, 80, 86, and 92 can be found, for example, at page 9, line 20 through page 10, line 4. Moreover, support for claims 35, 43, 70, 81, 87, and 93 can be found, for example, at page 17, lines 11-15, and support for claims 36, 44, 71, 82, 88, and 94 can be found, for example, at page 22, lines 13-21. Claims 37, 45, 72, 83, 89, and 95 find support, for example, at page 11, lines 12-13. Finally, support for claims 46-68, 73-79, 84-85, and 90-91 can be found, for example, at page 4, lines 9-28; page 9, line 20 through page 10, line 30; page 18, lines 5-6; page 43, original claim 1; and Figure 1.

No new matter has been added by way of this amendment. Entry of the amendment and remarks is respectfully requested.

Applicants wish to point out that a Second Preliminary Amendment was filed by Applicants on December 8, 1999 (*see, e.g.*, the attached copy of the Second Preliminary Amendment and the date stamped postcard showing receipt by the Patent Office). The Official Action of December 13, 2000 did not reflect the entry of this amendment. Applicants respectfully request that this amendment be made of record in the captioned application. Applicants note that some of the amendments to the specification which were requested in Applicants' Second Preliminary Amendment of December 8, 1999 (*e.g.*, changes at page 4, line 18; page 4, line 20; and page 4, line 26), showed the incorrect line numbers on page 4, and in some instances showed an incorrect length of amino acid residues. Therefore, Applicants have provided a clean version and a marked up version of the changes to the specification correctly reflecting these amendments.

The Restriction Requirement

The Examiner contends that the inventions are distinct, each from the other, and thus, has required an election under 35 U.S.C. § 121.

In order to be fully responsive, Applicants hereby provisionally elect the invention of Group I, drawn to polypeptides, with traversal. Applicants point out that the claims 14-15 have been cancelled and that new claims 21 to 95 are directed to subject matter falling within the scope of Group I as defined by the Examiner.

With respect to the Examiner's division of the invention into five (5) groups and the reasons stated therefor, Applicants respectfully traverse. Applicants submit that even where two patentably distinct inventions appear in a single application, restriction remains improper unless it can be shown that the search and examination of both groups would entail a "serious burden" (*See M.P.E.P.* § 803). In the present situation, no such showing has been made.

Even assuming, *arguendo*, that Groups I-V represent distinct or independent inventions, Applicants submit that to search and examine the subject matter of all the Groups

together would not be a serious burden on the Examiner. For example, as stated by the Examiner in the Office Action dated December 13, 2000, the protein of Group I is related to the antibody of Group II. Thus, Applicants submit that a search of the polypeptide claims would clearly provide useful information for the polynucleotide claims and antibody claims. In many, if not most publications, where a published polypeptide is described, the authors also include, as a matter of routine, a polynucleotide sequence encoding this polypeptide. Thus, Applicants submit that a search of antibody claims of the invention would provide useful information for examining claims directed to both polypeptides and the polynucleotides encoding these polypeptides. Further, Applicants point out that, in many if not most publications, where a published nucleotide sequence is an open reading frame, the authors also include, as a matter of routine, the deduced amino acid sequence of the encoded polypeptide.

Similarly, a search of the polypeptide claims of the invention would clearly provide useful information for the examination of claims directed to antibodies either produced in response to or having affinity for the subject polypeptides. This is because antibodies are frequently defined by the antigens that they are produced in response to and the epitopes to which they bind. Moreover, in many publications where an antibody is described, the antigen that it was produced in response to is also described.

Further, searches of publications directed to polypeptides and the use of those polypeptides would clearly be overlapping. This is so because in many, if not most, publications which describe polypeptides, these molecules are described by their function. Thus, a search of polypeptide claims would also provide the Examiner with art directed to the manner in which the claimed polypeptides could be used to in diagnostics, identification of agonists and antagonist of the polypeptides, and/or to treat disease states.

Accordingly, Applicants respectfully request that the restriction requirement under 35 U.S.C § 121 be reconsidered and withdrawn and the instant claims be examined in one application.

Applicants retain the right to petition from the restriction requirement under 37 C.F.R. § 1.144.

Applicants respectfully request that the above-made amendments and remarks be entered and made of record in the file history of the instant application. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: May 17, 2001

Michele M. Wales
Michele M. Wales (Reg. No. 43,975)
Attorney for Applicants

Human Genome Sciences, Inc.
9410 Key West Avenue
Rockville, MD 20850
Phone: (301) 610-5772
Fax: (301) 309-8439

MMW/CCB/ba

EXHIBIT

D



UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

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Washington, D.C. 20231

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|-----------------|-------------|----------------------|---------------------|
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09/393,023 09/09/99 MEISSNER

P PF-200

022195
HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE MD 20850

HM12/0706

EXAMINER

KAUFMAN, C

ART UNIT

PAPER NUMBER

1646

DATE MAILED:

07/06/01

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JUL 09 2001

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HGS PATENT DEPT.

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

| | | | |
|------------------------------|-------------------|-----------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 09/393,023 | MEISSNER ET AL. | |
| | Examiner | Art Unit | |
| | Claire M. Kaufman | 1646 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 May 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14, 16, 19-95 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 14, 16, 19-95 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Restriction Requirement:

Applicants election of Group I, now represented by claims 21-95 in paper number 10 filed 5/17/01, with traverse, is acknowledged. The traversal is on the ground(s) that the examination of the entire application would not constitute a burden to search because the Groups are related (e.g., antibody to polypeptide, polypeptide to polynucleotide). This is not found persuasive because contrary to Applicants' assertion that any search of the prior art in regard to Group I will reveal whether any prior art exists as to Group II-V (claims 14, 16, 19 and 20), a search is directed to references which would render the invention obvious, as well as references directed to anticipation of the invention, and therefore requires a search of relevant literature in many different areas of subject matter. For example, a search for the polypeptide must involve isolates produced by other than recombinant means. Also, nucleic acid references do not necessarily disclose a protein produced by translation of the nucleic acid. As to polypeptides and antibodies, the claimed antibodies are not required to bind only the claimed polypeptide fragment at the exclusion of other proteins. Therefore, the search for antibodies require more than searching the complete protein fragment of which it binds only a portion. For polypeptide compared to process claims, as pointed out above, a search is required for not only anticipatory references, but also those that would make obvious the invention, requiring non-coextensive searches. Therefore, restriction between groups is proper.

Applicants newly filed claims are drawn to numerous patentably distinct protein sequences and a method of producing the protein. Thus, further restriction *within* the formerly presented Group I is required, as follows:

The claims are drawn to numerous patentably distinct proteins, each of which constitutes a patentably distinct product. Applicants are required to elect a single invention of a protein, selected from the group consisting of: a protein comprising a polypeptide selected from the group consisting of the following regions of SEQ ID NO:2: Residues 1-223, 1-173, 24-223, 24-67, 24-173, 45-128, 68-173, 68-223, 129-207 and 174-223 (including polypeptides $\geq 90\%$ identical; i.e. elect one from the previous Markush group), and a single ultimate species of a

fragment of residues 1-223 which retains function (as in claim 21(k)), and a fragment of ≥ 30 amino acids of SEQ ID NO: 2.

Applicants should note that in some cases multiple claims encompass one of the patentably distinct inventions set forth herein, for example it is presumed by the Examiner in setting forth this requirement that the complete protein encoded by the cDNA of ATCC deposit 97142 is SEQ ID NO: 2. To be fully responsive to this requirement, Applicants are required to point out which claims correspond to the elected invention.

Although the classifications for these various proteins are overlapping, for instance 530/300, each represents a patentably distinct product with distinct physical and functional characteristics. Additionally, the burden of search for the Office has increased with multiple sequences because of the rapid introduction of new sequences to public sequence databases. Further the search for more than one product would be burdensome, because some are claimed not by protein sequence, but by the sequence encoded by a nucleic acid sequence, and requires a search of the corresponding region of SEQ ID NO: 1 as well as a 'reverse translation' search of the corresponding region of SEQ ID NO: 2, such that each individual sequence requires two sequence searches which are not required for any of the other sequences; or alternatively by virtue of comprising only a small portion of a disclosed protein, which requires a separate "word search" of the protein and/or nucleic acid databases, or by claiming proteins which are not 100% identical to a disclosed protein, which requires a broader search of the protein databases. Due to the use of 'comprising' language, it cannot even be said that the search for a protein comprising amino acids 1-223 of SEQ ID NO: 2 would reveal art pertaining to, for instance, a protein *comprising* amino acids 24-67 of SEQ ID NO: 2, as the latter could be found embedded in a completely different protein. Accordingly, restriction is proper.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(i).

Application/Control Number: 09/393,023
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Page 4

Conclusion


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.


Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. Please advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.


Patent Examiner, Art Unit 1646

July 5, 2001



EXHIBIT

E



VIA HAND DELIVERY SEPTEMBER 5, 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Meissner et al.

Application Number: 09/393,023

Filed: September 9, 1999

Title: Human Cripin Growth Factor

Group Art Unit: 1646

Examiner: Kaufman, C.

Attny. Docket No.: PF200D

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TECH CENTER 1600/2900

RESPONSE TO FURTHER RESTRICTION REQUIREMENT. PROVISIONAL
ELECTION. AND TRAVERSE UNDER 37 C.F.R. § 1.143

Commissioner for Patents and Trademarks
Washington, D.C. 20231

Sir or Madam:

In response to the Further Restriction Requirement mailed July 6, 2001, please enter the following provisional election, with traverse, and consider the remarks below. Applicants submit concurrently herewith: (a) a Petition for an Extension of Time for one (1) month, up to and including September 6, 2001; (b) a Fee Transmittal Sheet; and (c) Associate Power of Attorney.

Remarks

Claims 14, 16, and 19-95 are pending in the instant application.

Applicants request reconsideration and withdrawal of the present restriction requirement.

The Restriction Requirement

The Examiner appears to be requiring an election of "species" (i.e., sequence) within the provisionally elected Group I.

More particularly, the Examiner alleges:

The claims are drawn to numerous patentably distinct proteins, each of which constitutes a patentably distinct product. Applicants are required to elect a single invention of a protein, selected from the group consisting of: a protein comprising a polypeptide selected from the group consisting of the following regions of SEQ ID NO:2: Residues 1-223, 1-173, 24-223, 24-67, 24-173, 45-128, 68-173, 68-223, 129-207 and 174-223 (including polypeptides \geq 90% identical; i.e., elect one from the previous Markush group), and a single ultimate species of a fragment of residues 1-223 which retains

function (as in claim 21(k)), and a fragment of ≥ 30 amino acids of
SEQ ID NO:2.

(See, Paper No. 13, Pages 2-3, Paragraph 3.)

In order to be fully responsive, Applicants hereby elect, with traverse, an isolated protein comprising amino acids 24 to 173 of SEQ ID NO:2 (Claims 21(e), 26, 33, and 35-37). Applicants reserve the right to file one or more divisional applications directed to non-elected inventions should the additional restriction requirement be made final. In such a case, Applicants retain the right to petition from the additional restriction requirement under 37 C.F.R. § 1.144.

Applicants respectfully traverse and request the withdrawal of the requirement for further restriction.

As a threshold matter, Applicants point out that MPEP § 803 lists the criteria for a proper restriction requirement:

Under the statute an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are either independent (MPEP § 806.04 - § 806.04(i)) or distinct (MPEP § 806.05 - § 806.05(i)).

If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

Thus, even assuming, *arguendo*, that the sequences listed by the Examiner represent distinct or independent inventions, restriction remains improper unless it can be shown that the search and examination of these sequences would entail a "serious burden." See M.P.E.P. § 803. In the present situation no such showing has been made.

The Examiner has alleged that

Although the classifications for these various proteins are overlapping, for instance 530/300, each represents a patentably distinct product with distinct physical and functional characteristics. Additionally, the burden of search for the Office has increased with multiple sequences because of the rapid introduction of new sequences to public sequence databases. Further the search of more than one product would be burdensome, because some are claimed not by protein sequence, but by the sequence encoded by a nucleic acid sequence, and requires a search of the corresponding region of SEQ ID NO:1 as well as a 'reverse translation' search of the

corresponding region of SEQ ID NO:2, such that each individual sequence requires two sequence searches which are not required for any of the other sequences; or alternatively by virtue of comprising only a small portion of a disclosed protein, which requires a separate "word search" of the protein and/or nucleic acid databases, or by claiming proteins which are not 100% identical to a disclosed protein, which requires a broader search of the protein databases. Due to the use of 'comprising' language, it cannot even be said that the search for a protein comprising amino acids 1-223 of SEQ ID NO:2 would reveal art pertaining to, for instance, a protein *comprising* amino acids 24-67 of SEQ ID NO:2, as the latter could be found embedded in a completely different protein. Accordingly, restriction is proper.

(See, Paper No. 13, Page 3, Paragraph 5, emphasis in original.)

Applicants disagree and submit that an art search with a protein comprising amino acid residues 24 to 173 of SEQ ID NO:2 would be largely overlapping with that for a protein comprising amino acid residues 1-223, 1-173, 24-223, 24-67, 45-128, 68-173, 68-223, 129-207, or 174-223 of SEQ ID NO:2 (including polypeptides \geq 90% identical to those fragments), a fragment of residues 1-223 which retains function, and a fragment of \geq 30 amino acids of SEQ ID NO:2. Thus, the search and examination of all claims which encompass a protein comprising amino acid residues 1-223, 1-173, 24-223, 24-67, 24-173, 45-128, 68-173, 68-223, 129-207, or 174-223 of SEQ ID NO:2 (including polypeptides \geq 90% identical to those fragments), a fragment of residues 1-223 which retains function, and a fragment of at least 30 contiguous amino acids of SEQ ID NO:2 would not entail a serious burden.

In addition, Applicants respectfully remind the Examiner that upon allowance of a generic claim, Applicants will be entitled to the consideration of additional "species" which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141. MPEP § 809.02(a).

Thus, Applicants respectfully request that the further restriction within the formerly presented Group I be withdrawn so the restricted subject matter can be examined together.

Applicants respectfully point out that the provisionally elected claim 21(e) is overlapping in scope to the pending claims, particularly given that all of the claims are directed to SEQ ID NO:2 (or the corresponding deposited clone). Nevertheless, to the extent that the Examiner requests that Applicants "point out which claims correspond to the elected

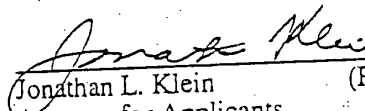
invention" (see, Paper No. 13, Page 3), Applicants point out that claims 26, 33, and 35-37 are particularly directed to the provisionally elected subject matter of claim 21(e).

Conclusion

Applicants respectfully request that the above-made remarks be entered and made of record in the file history of the instant application. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: SEPTEMBER 5, 2001


Jonathan L. Klein (Reg. No. 41,119)
Attorney for Applicants

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Phone: (301) 251-6015
Fax: (301) 309-8439

MMW/JKE/CCB/ba



EXHIBIT

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UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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Washington, D.C. 20231
www.uspto.gov



| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/393,023 | 09/09/1999 | PAUL S. MEISSNER | PF-200 | 2146 |

22195 7590 11/26/2001

HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE, MD 20850

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MMW CB

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EXAMINER

KAUFMAN, CLAIRE M

| ART UNIT | PAPER NUMBER |
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1646

DATE MAILED: 11/26/2001

17

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|-------------------|-----------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 09/393,023 | MEISSNER ET AL. | |
| | Examiner | Art Unit | |
| | Claire M. Kaufman | 1646 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09/09/99, 12/08/99, 05/17/01.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14, 16 and 19-95 is/are pending in the application.
- 4a) Of the above claim(s) 14, 16, 19, 20, 22-25, 27-32, 34 and 38-95 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21, 26, 33 and 35-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 14, 16 and 19-95 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 September 1999 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>2, 11</u> . | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

The amendments filed 9/9/99, 12/8/99 and 5/17/01 have been entered.

Election/Restrictions

Applicant's election with traverse of Group I of protein comprising amino acids 24-173 of SEQ ID NO:2 in Paper No. 16 is acknowledged. The traversal is on the ground(s) that 1) this should be/is a species election with additional species being examined if the first species is found allowable, 2) there is no serious burden of search for examining multiple sequences. This is not found persuasive.

With respect to Applicants' first point, although the word "species" was used in the restriction of 7/6/01, it was not a "species" restriction/election. Each embodiment set forth in the restriction is a distinct and separate invention. There is no generic claim since art against a fragment would not constitute art against the full-length protein, and the art against one fragment would not necessarily constitute art against another. As a result, only one invention will be examined: a protein comprising amino acids 24-173 of SEQ ID NO:2.

With respect to Applicants' second point, there is a serious burden of search for searching the multiple sequences/proteins claimed. Some fragments are short and need to be only 90% identical to a disclosed fragment, so the sequence could be embedded within other patentably distinct proteins. Therefore, it cannot be said that they are merely fragments of a common protein. A separate search is required for each possible fragment. Searching the full-length protein sequence will not necessarily result in the identification of art pertinent to the fragments since the USPTO search system generally has a limited number of "hits" saved and the burden of search for the Office has increased with multiple sequences because of the rapid introduction of new sequences to public sequence databases.

The requirement is still deemed proper and is therefore made FINAL.

The elected invention is a protein comprising a polypeptide having an amino acid sequence of residues 24-173 of SEQ ID NO: 2. Thus, claims 21, 26, 33 and 35-37 as they are

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drawn to the elected invention are under consideration. Claims 14, 16, 19, 20, 22-25, 27-32, 34 and 38-95 are withdrawn from prosecution as being drawn to a non-elected invention.

Drawings

The corrected or substitute drawings were received on 12/8/99. These drawings are approved.

Response to Amendment

The Declaration under 37 CFR 1.132 filed 12/8/99 is sufficient to address potential issues of new matter relating to the sequence differences between this and the parent application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21, 26, 33 and 35-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 32 of U.S. Patent No. 5,981,215. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claims encompass the protein encoded by the cDNA clone contained in ATCC No. 97142. Further, it would have been obvious to express the cDNA in a host cell, recovering the protein which can be glycosylated depending on the type of host cell. Such a protein is generally recovered in a buffer, a pharmaceutically acceptable carrier. It further would have been obvious for the protein to further comprise a heterologous polypeptide

which functioned as a purification tag, for example, because it was well known that the many commercially available protein purification tags were valuable tools at the time the instant invention was made (see also claim 42 and 47 of US Patent No. 5,981,215).

Claim Objections

Claims 21, 33 and 35-37 are objected to for encompassing multiple patentably distinct inventions. The claims should be amended to include only the elected invention. Correction is required.

Objections and Rejections under 35 U.S.C. §§101 and 112

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 21, 26, 33 and 35-37 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility.

The utility set forth in the specification p.17, last paragraph, is that of pancreatic cancer diagnosis. This is based on "An initial Northern blot analysis [that] has shown very high expression in pancreatic cancer cells." For several reasons this is not a specific or substantial utility. First, it is not known how the level of expression compares to expression in normal noncancerous cells, nor if the expression was analyzed in cell cultures or in cancerous tissue. Markers for cell lines are not necessarily representative of primary cell cultures or tissue since it is well known that cells can undergo changes in expression when cultured for extended passages. Also, a cancer cell line is representative of only a single sample (cell lines originate from 1 patient's cells), which is not enough information to conclude that protein alteration in that cell line is a universal phenomenon in all or most pancreatic cell samples. Second, polynucleotide expression is not necessarily indicative of protein expression. There is no information on altered level of protein (the claimed product) in pancreatic cancer cells.

The specification teaches that the mature criptin protein (amino acids 24-223 of SEQ ID NO:2) has the putative activity of wound healing and stimulation of vasculogenesis (p. 18, 3rd and 4th full paragraph). The prior art teaches a structurally related protein called "cripto" which has been identified as a cancer marker (p. 2, third paragraph; and references AA and AE), as well as a related gene called "CR-3" (AB), the function of which is also unknown. Neither of these prior art proteins is disclosed as having a transmembrane domain, although criptin is disclosed as having a transmembrane domain (p. 4, 8 lines from bottom). In the current instance the nature of the invention is largely unknown since the related prior art proteins have no described function except as tumor cell markers and have a conserved "EGF motif" which confers some structural form. There are no examples of criptin promoting wound healing or vasculogenesis. The list of tissue in which it may promote wound healing is diverse: skin, bone, muscle, lung..., and no specific tissue is identified nor under what circumstances criptin can actually promote wound healing (*e.g.*, cellular state of tissue--proliferating or differentiating, effective amount, or *in vivo* compared to *in vitro* activity). Also, the currently claimed protein has several putative functions listed and a putative three dimensional structure, but without information on the relationship of structure to function.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 26, 33 and 35-37 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the means by which the protein can be produced. There is nothing to indicate the host cell anything by which it can produce the protein, for example, a nucleic acid encoding the protein.

Claim 37 is indefinite because in step (b), it is unclear if "the protein" recovered is said isolated protein of claim 21 or if it is another protein in/from the cell.

Claim 34 is indefinite for failing to indicate the relationship between the recited structural elements. Specifically, it is not clear how the "heterologous polynucleotide" of claim 34, for example, relates to the polynucleotide of claim 21. In claim 34, it is not clear whether the heterologous sequence is attached at an end or might be internally inserted.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. Please advise the examiner at the telephone number above before facsimile transmission.

Application/Control Number: 09/393,023

Page 7

Art Unit: 1646

Claire M. Kaufman, Ph.D.

A handwritten signature in cursive script, reading "Claire M. Kaufman". The signature is written in dark ink and is positioned above the printed name and title.

Patent Examiner, Art Unit 1646

November 15, 2001

EXHIBIT

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Washington, DC 20231

RJH

Paper No. 22

In re Application of:
MEISSNER ET AL.
Serial No.: 09/393,023
Filed: September 09, 1999
For: Human Criptin Growth Factor

DECISION ON PETITION

This is a decision on the petition under 37 CFR 1.144, filed March 27, 2002, to withdraw the restriction requirement.

Initially it is noted that on April 11, 2002, a petition decision was inadvertently mailed to applicants. That decision was mailed prematurely. Consequently, that decision is hereby vacated in favor of this decision. Any confusion or problems caused by this inadvertent mailing is sincerely regretted.

Status of Application

On December 13, 2000, a restriction requirement was mailed to applicants. On May 17, 2001, applicants elected an invention with traverse, canceled claims 1-13, 15, and 17-18, and added new claims 21-95. On July 6, 2001, another restriction requirement was mailed to applicants in view of the many new claims added by the May 17, 2001 paper. On September 5, 2001, applicants again elected an invention with traverse. On November 26, 2001, a non-final Office action was mailed to applicants that rebutted applicants' traversal of the restriction requirement and made the restriction final. On March 27, 2002, the present petition was filed.

Petitioner's Arguments

Petitioner asserted that the restriction requirement is improper because the examiner failed to consider whether the claimed inventions were "independent" as required by the plain and unambiguous meaning of 35 U.S.C. § 121, and asserts that the examiner improperly concluded that the separately claimed inventions are "distinct." Specifically, petitioner notes that 35 U.S.C. § 121 states (emphasis added):

If two or more independent and distinct inventions are claimed in one application, the Director may require the application to be restricted to one of the inventions.

From this, petitioner concluded that while the examiner presented reasons why the inventions are "distinct," the examiner did not present any reasons why the inventions were "independent" and, therefore, the examiner did not meet the statutory requirement for restriction.

Petitioner also argued that even if the inventions only have to be distinct from each other for the restriction to be proper, in this case the inventions restricted from each other, a full length sequence and fragments and variants of the sequence, are related as combination and subcombination inventions. As such, two-way distinctness is required. The petition puts it this way:

The full-length claims and the fragment and variant claims are not "two-way" distinct. For example, if the polypeptide of the full-length claims (i.e., the combination) was known in the art before the invention of the polypeptides of the fragment and variant claims (the subcombination claims), the subcombinations would not be patentable as claimed. This is because the full-length sequence would anticipate the fragment and variant claims. Thus, the Examiner erred in concluding that claims 21-95 are patentably distinct.

To support this position, petitioner includes on page 5 of the petition a quote from the USPTO that discusses viewing genes and nucleic acids as being combinations of sequences that are subcombinations. See page 5 of the petition as well as Exhibit G of the petition.

Response to Petitioner's Arguments

The argument regarding "independent and distinct" is not persuasive. The MPEP makes it clear that the USPTO interprets the "independent and distinct" language of the statute in such a way that restriction is proper as long as the inventions are independent or as long the inventions are distinct. In other words, the USPTO interprets the "independent and distinct" language of the statute as "independent or distinct". See the explanation provided in MPEP section 802.01. Furthermore, it is noted that applicant's prior replies to the restriction requirement acknowledged that the standard for restriction requires independent or distinct inventions and a serious search burden. See page 2 of paper filed 9/5/01 and pages 13-14 of paper filed 5/17/01.

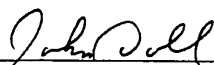
However, in reviewing the restriction requirement as a result of petitioner's remaining arguments, it was determined that the Groups as presented by the examiner were not entirely independent from each other or patentably distinct from each other. Consequently, the petition is hereby granted to the extent that the restriction requirement as it currently stands and the last Office action (dated November 26, 2001) are hereby

Application Serial No. 09/393,C
Technology Center 1600

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vacated. The application has been forwarded to the examiner for appropriate action consistent with this decision, e.g., a new restriction requirement.

PETITION GRANTED but only to the extent that the restriction requirement as it currently stands and the last Office action (dated November 26, 2001) are hereby vacated.



John Doll, Director
Technology Center 1600

HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE, MD 20850

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EXHIBIT

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UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/393,023 | 09/09/1999 | PAUL S. MEISSNER | PF-200 | 2146 |



22195 7590 06/19/2002
HUMAN GENOME SCIENCES INC
19410 KEY WEST AVENUE
ROCKVILLE, MD 20850

EXAMINER

KAUFMAN, CLAIRE M

ART UNIT PAPER NUMBER

1646

DATE MAILED: 06/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | | |
|------------------------------|--------------------------------------|--|--|--|
| Office Action Summary | Application No. 09/393,023 | | Applicant(s) MEISSNER ET AL. | |
| | Examiner Claire M. Kaufman | | Art Unit 1646 | |
| | | | | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 26 March 2002.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 14, 16 and 19-95 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☐ Claim(s) _____ is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claim(s) 14, 16, and 19-95 are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

| | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

Claims 21-95 are directed to the following inventions:

1. Isolated proteins comprising amino acid residues 1-223 of SEQ ID NO:2
2. Isolated proteins comprising amino acid residues 1-173 of SEQ ID NO:2 except for those proteins comprising amino acid residues 1-223 of SEQ ID NO:2.
3. Isolated proteins comprising amino acid residues 24-223 of SEQ ID NO:2 except for those proteins comprising amino acid residues 1-223 of SEQ ID NO:2
4. Isolated proteins comprising amino acid residues 24-67 of SEQ ID NO:2 except for those proteins comprising amino acid residues 24-173 of SEQ ID NO:2, those proteins comprising amino acid residues 1-173 of SEQ ID NO:2, those proteins comprising amino acid residues 24-223 of SEQ ID NO:2, and those proteins comprising amino acid residues 1-223 of SEQ ID NO:2
5. Isolated proteins comprising amino acid residues 24-173 of SEQ ID NO:2 except for those proteins comprising amino acid residues 24-223 of SEQ ID NO:2, those proteins comprising amino acid residues 1-173 of SEQ ID NO:2, and those proteins comprising amino acid residues 1-223 of SEQ ID NO:2
6. Isolated proteins comprising amino acid residues 45-128 of SEQ ID NO:2 except for those proteins comprising amino acid residues 24-173 of SEQ ID NO:2, those proteins comprising amino acid residues 1-173 of SEQ ID NO:2, those proteins comprising amino acid residues 24-223 of SEQ ID NO:2, and those proteins comprising amino acid residues 1-223 of SEQ ID NO:2
7. Isolated proteins comprising amino acid residues 68-173 of SEQ ID NO:2 except for those proteins comprising amino acid residues 24-173 of SEQ ID NO:2, those proteins comprising amino acid residues 1-173 of SEQ ID NO:2, those proteins comprising amino acid residues 24-223 of SEQ ID NO:2, and those proteins comprising amino acid residues 1-223 of SEQ ID NO:2
8. Isolated proteins comprising amino acid residues 68-223 of SEQ ID NO:2 except for those proteins comprising amino acid residues 24-223 of SEQ ID NO:2 and those proteins comprising amino acid residues 1-223 of SEQ ID NO:2
9. Isolated proteins comprising amino acid residues 129-207 of SEQ ID NO:2 except for those proteins comprising amino acid residues 68-223 of SEQ ID NO:2, those proteins comprising amino acid residues 24-223 of SEQ ID NO:2, and those proteins comprising amino acid residues 1-223 of SEQ ID NO:2

10. Isolated proteins comprising amino acid residues 174-223 of SEQ ID NO:2 except for those proteins comprising amino acid residues 68-223 of SEQ ID NO:2, those proteins comprising amino acid residues 24-223 of SEQ ID NO:2, and those proteins comprising amino acid residues 1-223 of SEQ ID NO:2
11. Isolated proteins comprising a polypeptide fragment of amino acids 1-223 of SEQ ID NO:2 wherein the polypeptide fragment stimulates cell growth and is not any of the fragments listed in claim 21(a)-21(j).
12. Isolated proteins comprising an amino acid sequence 90% or more but not 100% identical to amino acid residues 1-223 of SEQ ID NO:2
13. Isolated proteins comprising an amino acid sequence 90% or more but not 100% identical to amino acid residues 1-173 of SEQ ID NO:2
14. Isolated proteins comprising an amino acid sequence 90% or more but not 100% identical to amino acid residues 24-223 of SEQ ID NO:2
15. Isolated proteins comprising an amino acid sequence 90% or more but not 100% identical to amino acid residues 24-67 of SEQ ID NO:2
16. Isolated proteins comprising an amino acid sequence 90% or more but not 100% identical to amino acid residues 24-173 of SEQ ID NO:2
17. Isolated proteins comprising an amino acid sequence 90% or more but not 100% identical to amino acid residues 45-128 of SEQ ID NO:2
18. Isolated proteins comprising an amino acid sequence 90% or more but not 100% identical to amino acid residues 68-173 of SEQ ID NO:2
19. Isolated proteins comprising an amino acid sequence 90% or more but not 100% identical to amino acid residues 68-223 of SEQ ID NO:2
20. Isolated proteins comprising an amino acid sequence 90% or more but not 100% identical to amino acid residues 129-207 of SEQ ID NO:2
21. Isolated proteins comprising an amino acid sequence 90% or more but not 100% identical to amino acid residues 173-223 of SEQ ID NO:2
22. Isolated proteins comprising an amino acid sequence 90% or more but not 100% identical to a polypeptide fragment of amino acids 1-223 of SEQ ID NO:2 wherein the polypeptide fragment stimulates cell growth and is not any of the fragments listed in claim 46(a)-46(j)
23. Isolated proteins comprising at least 30 contiguous amino acids of SEQ ID NO:2 but wherein the at least 30 contiguous amino acids are not any of the fragments listed in claim 21(a)-21(j)

The remaining claims are directed to the following inventions:

- 24. Claim 14, drawn to a compound that inhibits specific polypeptides, classified in class 530, subclass 388.24.
- 25. Claim 16, drawn to a process for identifying compounds that inhibit specific polypeptides, classified in class 435, subclass 7.21.
- 26. Claim 19, drawn to a process for diagnosing a disease by mutation analysis, classified in class 435, subclass 6.
- 27. Claim 20, drawn to a method of detecting polypeptide presence, classified in class 435, subclass 7.1, for example (classification is dependent on the method steps).

The inventions are independent or distinct from each other for the following reasons:

Each of Groups 1-23 is directed to isolated proteins wherein the proteins of each Group differ in structure relative to the proteins of each of the other Groups. Because of the difference in structure between the isolated proteins of each of the Groups, they are not related to each other (i.e., they are independent) and would be expected to have different properties and characteristics from each other.

Each of Groups 1-23 is independent from the compounds of Group 24. Specifically, each of Groups 1-23 is directed to isolated proteins whereas Group 24 is directed to inhibitor compounds that do not even have to be protein.

Each of Groups 1-23 is independent from each of the methods of Groups 25-27 since none of the methods make, use, or are otherwise related to the proteins in Groups 1-23.

The compounds of Group 24 are related to the method of Group 25 only insofar as the method of Group 25 can be used to identify the compounds of Group 24. However, these inventions are distinct from each other because the compounds of Group 24 could be identified using a method other than that of Group 25, such as a non-cellular method.

The compounds of Group 24 are independent from the methods of Groups 26-27 because there is no relationship whatsoever between these Groups, i.e., the methods of Groups 26-27 do not make, use, or identify the compounds of Group 24.

The methods of Groups 25-27 are independent from each other because they each require different method steps and obtain different results.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and

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Art Unit: 1646

the search required for one group is not coextensive with any other, restriction for examination purposes as indicated is proper.

If applicants elect one of Groups 1-23, applicants are also required to list all the claims readable on the elected invention. Note, this is not an election of species requirement but a restriction between independent or distinct inventions. Note also that if applicants elect one of Groups 1-23, rejoinder of certain groups will be considered depending on the results of the search and examination and as long as there is no burden in examining the groups together in one application.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman whose telephone number is 703-308-5791. Dr. Kaufman can normally be reached on Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. Please advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.



Patent Examiner, Art Unit 1646

June 10, 2002

EXHIBIT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Meissner et al.

Application Number: 09/393,023

Group Art Unit: 1646

Filed: September 9, 1999

Examiner: Kaufman, C.

Title: Human Criptin Growth Factor

Attny. Docket No.: PF200D1

**RESPONSE TO RESTRICTION REQUIREMENT (PAPER NO.23), PROVISIONAL
ELECTION, AND TRAVERSE UNDER 37 C.F.R. § 1.143**

Commissioner for Patents and Trademarks
Washington, D.C. 20231

Sir:

In response to the Restriction Requirement mailed June 19, 2002, please enter the following provisional election, with traverse, and consider the remarks below. Applicants submit concurrently herewith: (a) a Petition for an Extension of Time for two (2) months, up to and including September 19, 2002; and (b) a Fee Transmittal Sheet.

Remarks

Claims 14, 16, and 19-95 are pending in the instant application.

Applicants respectfully traverse the restriction requirement set forth in Paper No.23 for the reasons stated in the petition under 37 C.F.R. §§ 1.144 and 1.181(c) submitted herewith, which is hereby incorporated by reference.

In a conference with John Doll, the Director of Group 1600, Applicants were informed that they could submit the instant petition with the preliminary election with traverse. Therefore, it was Applicants' understanding that, even though the Examiner has not yet deemed the restriction requirement final, the instant petition would nonetheless be considered timely filed.

Provisional Election

The Examiner has required an election under 35 U.S.C. § 121 of one of twenty-seven groups cast by the Examiner. *See* Paper No. 23, pages 2-5. The Examiner contends that each group set out by the Examiner is independent of the others. In order to be fully responsive, Applicants hereby elect, with traverse, the subject matter of Group 1, *i.e.*, an isolated protein comprising amino acids 1 to 223 of SEQ ID NO:2 (represented by claims 21(a), 22, 32-33, and 35-37). To the extent that the Examiner requests that Applicants "list all claims readable on the elected invention" (*see* Paper No. 23, page 5), Applicants point out that claims 21-95 are readable on the elected invention

Applicants reserve the right to file one or more divisional applications directed to non-elected inventions should the additional restriction requirement be made final. In such a case, Applicants retain the right to petition from the restriction requirement under 37 C.F.R. § 1.144.

Conclusion

Applicants respectfully request that the above-made remarks be entered and made of record in the file history of the instant application. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Dated: 19 Sept. 2002

Charles E. Van Horn
Charles E. Van Horn
Reg. No. 40,266

EXHIBIT

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UNITED STATES PATENT AND TRADEMARK OFFICE

RESTRICTION PRACTICE FOR MARKUSH AND SEQUENCE CLAIMS

Action:

Markush claims and sequence claims present huge search and examination challenges when the number of species or sequences claimed in one application, and many times in one claim, exceed hundreds, thousands or even gazillions of compounds and sequences. Current restriction practice under 37 CFR 1.142 needs to be clarified to specifically address the restriction to a single independent and distinct invention within a Markush claim and the restriction to a single and distinct polypeptide or DNA sequence.

Background Information:

Applications in organic chemistry frequently claim a myriad of chemical species in a single Markush¹ type claim. Even though these compounds have a common utility and one of ordinary skill in the art would know how to make and use any of them, these claims pose a tremendous challenge in doing a complete search and examination. They encompass numerous classes and subclasses and structurally divergent chemical compounds.

Applications in biotechnology frequently claim tens, hundreds or thousands of nucleotide and/or amino acid sequences in a single application and many times in a single claim. Each and every nucleotide and/or amino acid sequence, even if they are all isolated from the same source, are independent and distinct for restriction purposes.

Regardless of the restriction requirement within a Markush claim or between biologic sequences, rejoinder of process claims that are commensurate in scope and include all the limitations of the elected product claim would be permissible under *In re Ochiai*, 71 F.3d 1565, 37 USPQ2d 1127 (Fed. Cir. 1995).

Options Considered:

Option 1 - Constructive Restriction/Election: Amend 37 CFR 1.142 to permit the restriction and constructive election of the first claimed independent and distinct species in a Markush claim or first claimed independent and distinct sequence in a biologic claim encompassing numerous sequences.

Advantages: Significantly reduces patent pendency by eliminating the time lost in telephonic or written restrictions before the actual examination on the merits of the application begins. A majority of organic chemistry and biotechnology applications have restriction requirements made before actual examination begins.

¹ Ex parte Markush, 1925 Dec. Comm'r Pat. 126 (1924).

UNITED STATES PATENT AND TRADEMARK OFFICE

Improves the quality of examination by reducing the number of inventions searched and examined, increases the time available to search and examine each invention, and focuses the prosecution on one inventive concept.

Option 2 – Written or Telephonic Restriction/Election: Amend 37 CFR 1.142 to codify the restriction and election of a single independent and distinct species within a Markush claim or a single independent and distinct sequence in a biologic claim encompassing numerous sequences.

Advantages: Codifies the current restriction practice and simplifies the search and examination procedures.

Improves the quality of examination by reducing the number of inventions searched and examined, increases the time available to search and examine each invention, and focuses the prosecution on one inventive concept.

USPTO Recommended Course of Action:

Option 1 - Constructive Restriction/Election in Markush and Sequence Claims.

Details:

Applicants original presentation of claims would determine the first claimed invention to be searched and examined. Rather than allowing the examiner to determine the first claimed invention by the claim construction, applicant (anticipating a restriction requirement) could also provisionally elect an independent and distinct species at the time of filing the application.

An application not only claiming products but also claiming processes of making and processes of using the products may also be restricted to the one independent and distinct product with the process claims being withdrawn from consideration. Rejoinder of any withdrawn process claims that are commensurate in scope and include all the limitations of the allowable elected product claim would be considered under *In re Ochiai*.

Timing:

Both options require Rule Making.

EXHIBIT

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Figure 1 shows the cDNA and corresponding deduced amino acid sequence of the polypeptide of the present invention. The standard one letter abbreviations for amino acids are used. Sequencing was performed using a 373 Automated DNA sequencer (Applied Biosystems, Inc.).

Figure 2 shows the amino acid sequence homology between the polypeptide of the present invention (top line) and the cripto growth factor (bottom line).

In accordance with an aspect of the present invention, there are provided isolated nucleic acids (polynucleotides) which encode for the mature polypeptide having the deduced amino acid sequence of Figure 1 (SEQ ID NO:2) or for the mature polypeptide encoded by the cDNA of the clone(s) deposited as ATCC Deposit No. 97142 on May 11, 1995.

A polynucleotide encoding a polypeptide of the present invention was discovered in a cDNA library derived from human pancreatic cancer tissue. It is structurally related to the human cripto growth factor. It contains an open reading frame encoding a protein of 230 amino acid residues of which approximately the first 23 amino acids residues are the putative leader sequence such that the mature protein comprises 207 amino acids. As shown in figure 2 the polypeptide of the present invention has conserved cysteine residues in common with cripto growth factor.

Moreover, the polypeptide of the present invention has a putative soluble portion comprising amino acid 45 to amino acid 128 of SEQ ID NO:2, such that amino acid 129 to amino acid 207 is a putative transmembrane portion.

An initial Northern blot analysis has shown very high expression in pancreatic cancer cells.

The polynucleotide of the present invention may be in the form of RNA or in the form of DNA, which DNA includes cDNA, genomic DNA, and synthetic DNA. The DNA may be double-stranded or single-stranded, and if single stranded may be the coding strand or non-coding (anti-sense) strand. The

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which are lacking certain amino acid residues yet still retain biological activity. Such fragments, derivatives and analogs are deemed to be within the scope of those skilled in the art from the teachings herein.

The polypeptides and polynucleotides of the present invention are preferably provided in an isolated form, and preferably are purified to homogeneity.

The term "isolated" means that the material is removed from its original environment (e.g., the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or polypeptide, separated from some or all of the coexisting materials in the natural system, is isolated. Such polynucleotides could be part of a vector and/or such polynucleotides or polypeptides could be part of a composition, and still be isolated in that such vector or composition is not part of its natural environment.

The polypeptides of the present invention include the polypeptide of SEQ ID NO:2 (in particular the mature polypeptide) as well as polypeptides which have at least 70% similarity (preferably at least a 70% identity) to the polypeptide of SEQ ID NO:2 and more preferably at least a 90% similarity (more preferably at least 90% identity) to the polypeptide of SEQ ID NO:2 and still more preferably at least a 95% similarity (still more preferably at least a 95% identity) to the polypeptide of SEQ ID NO:2 and also include portions of such polypeptides with such portion of the polypeptide generally containing at least 30 amino acids and more preferably at least 50 amino acids.

As known in the art "similarity" between two polypeptides is determined by comparing the amino acid sequence and its conserved amino acid substitutes of one polypeptide to the sequence of a second polypeptide.

EXHIBIT

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FOR FURTHER INFORMATION CONTACT: Dr. Subhas G. Malghan, FQA Program Manager, Building 820, Room 306, NIST, Gaithersburg, MD 20899; telephone (301) 975-5120, fax (301) 975-5414, E-mail: malghan@nist.gov.

SUPPLEMENTARY INFORMATION: On June 1, 1998, NIST announced in the *Federal Register*, (63 FR 29702), that it would be holding a public meeting on June 16, 1998, to provide details and interpretations on the regulations related to the Quality Assurance System (QAS) of fastener manufacturing contained in the April 14, 1998, final regulation under the Fastener Quality Act. NIST is postponing that meeting and will issue a future notice announcing a new date for the meeting.

Dated: June 10, 1998.

Robert E. Hebner,
Acting Deputy Director, National Institute of Standards and Technology.

[FR Doc. 98-15935 Filed 6-12-98; 8:45 am]

BILLING CODE 3510-13-M

DEPARTMENT OF COMMERCE

Patent and Trademark Office

[Docket No. 980605148-8148-01]

Request for Comments on Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶1 "Written Description" Requirement

AGENCY: Patent and Trademark Office, Commerce.

ACTION: Notice and request for public comments.

SUMMARY: The Patent and Trademark Office (PTO) requests comments from any interested member of the public on the following interim guidelines. These guidelines will be used by PTO personnel in their review of biotechnological patent applications for compliance with the "written description" requirement of 35 U.S.C. 112 ¶ 1. Although the guidelines are directed primarily to written descriptions of biotechnological inventions, they reflect the current understanding of the PTO and apply across the board to all relevant technologies.

DATES: Written comments on the interim guidelines will be accepted by the PTO until September 14, 1998.

ADDRESSES: Written comments should be addressed to Box 8, Commissioner of Patents and Trademarks, Washington, D.C. 20231, marked to the attention of Scott A. Chambers, Associate Solicitor or to Box Comments, Assistant Commissioner for Patents, Washington,

D.C. 20231 marked to the attention of Linda S. Therkorn. Alternatively, comments may be submitted to Scott Chambers via facsimile at (703) 305-9373 or by electronic mail addressed to "scott.chambers@uspto.gov" or to Linda Therkorn via facsimile at (703) 305-8825 or by electronic mail addressed at "linda.therkorn@uspto.gov."

FOR FURTHER INFORMATION CONTACT: Scott Chambers by telephone at (703) 305-9035, by facsimile at (703) 305-9373, by mail to his attention addressed to Box 8, Commissioner of Patents and Trademarks, Washington, D.C. 20231, or by electronic mail at "scott.chambers@uspto.gov"; or Linda Therkorn by telephone at (703) 305-8800, by facsimile at (703) 305-8825, by mail addressed to Box Comments, Assistant Commissioner for Patents, Washington, D.C. 20231, or by electronic mail at "linda.therkorn@uspto.gov."

SUPPLEMENTARY INFORMATION: The PTO requests comments from any interested member of the public on the following interim guidelines. These guidelines will be used by PTO personnel in their review of biotechnological patent applications for compliance with the "written description" requirement of 35 U.S.C. 112 ¶ 1. Although the guidelines are directed primarily to written descriptions of biotechnological inventions, they reflect the current understanding of the PTO and apply across the board to all relevant technologies. Because these guidelines govern internal practices, they are exempt from notice and comment rulemaking under 5 U.S.C. 553(b)(A).

Written comments should include the following information: (1) name and affiliation of the individual responding; and (2) an indication of whether the comments offered represent views of the respondent's organization or are they respondent's personal views. The PTO is particularly interested in comments relating to: (1) the accuracy of the methodology; (2) relevant factors to consider in determining whether the written description requirement of 35 U.S.C. 112 ¶ 1 is satisfied; (3) whether the scope of these guidelines should be limited to certain technologies, such as biotechnology, or even a particular area of biotechnology such as nucleic acids, or encompass all technologies generally; (4) whether the scope of these guidelines should be expanded to include processes and/or product-by-process claims; and (5) the impact these guidelines may have on currently pending applications as well as future applications.

Parties presenting written comments are requested, where possible, to provide their comments in machine-readable format in addition to a paper copy. Such submissions may be provided by electronic mail messages sent over the Internet, or on a 3.5" floppy disk formatted for use in either a Macintosh, Windows, Windows for Workgroups, Windows 95, Windows NT, or MS-DOS based computer.

Written comments will be available for public inspection on or about September 14, 1998, in Suite 918, Crystal Park 2, 2121 Crystal Drive, Arlington, Virginia. In addition, comments provided in machine-readable format will be available through anonymous file transfer protocol (ftp) via the Internet (address: comments.uspto.gov) and through the World Wide Web (address: www.uspto.gov).

Interim Guidelines for the Examination of Patent Applications Under The 35 U.S.C. 112 ¶1 "Written Description" Requirement

These "Written Description Guidelines" are intended to assist Office personnel in the examination of patent applications for compliance with the written description requirement of 35 U.S.C. 112, ¶ 1, in view of *University of California v. Eli Lilly*¹ and the earlier cases *Fiers v. Revel*² and *Amgen, Inc. v. Chugai Pharmaceutical Co.*³ These Interim Guidelines are directed primarily to determining whether there is written description support for product claims and are not intended to specifically address the description necessary to support process or product-by-process claims. Similarly, these Guidelines are not intended to directly address the question of new matter, which is currently addressed in the Manual of Patent Examining Procedure §§ 2163.06-.07. The Final Guidelines may address these additional issues if public comment suggests they should be addressed. These guidelines are based on the Office's current understanding of the law and are believed to be fully consistent with binding precedent of the Supreme Court, the Federal Circuit, and the Federal Circuit's predecessor courts.

These guidelines do not constitute substantive rulemaking and hence do not have the force and effect of law. They are designed to assist Office personnel in analyzing claimed subject matter for compliance with substantive law. Rejections will be based upon the substantive law, and it is these rejections which are appealable. Consequently, any failure by Office personnel to follow the guidelines is neither appealable nor petitionable.

These guidelines are intended to form part of the normal examination process. Thus, where Office personnel establish a *prima facie* case of lack of written description for a claim, a thorough review of the prior art and examination on the merits for compliance with the other statutory requirements, including those of 35 U.S.C. 101, 102, 103, and 112, is to be conducted prior to completing an Office action which includes a rejection for lack of written description.

Office personnel are to rely on these guidelines in the event of any inconsistent treatment of issues involving the written description requirement between these guidelines and any earlier guidance provided from the Office. Although these guidelines address examples principally drawn from the biotechnological arts, they are intended to be equally applicable to all fields of invention.

I. General Principles Governing Compliance with the "Written Description" Requirement for Applications

The first paragraph of 35 U.S.C. 112 requires that the "specification shall contain a written description of the invention * * *". This requirement is separate and distinct from the enablement requirement.⁴ This written description requirement has several policy objectives. "[T]he 'essential goal' of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed."⁵ Another objective is to put the public in possession of what the applicant claims as the invention. The written description requirement prevents an applicant from claiming subject matter that was not described in the specification as filed, and the proscription against the introduction of new matter in a patent application⁶ serves to prevent an applicant from adding information that goes beyond the subject matter originally filed.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.⁷ This requirement of the Patent Act promotes the progress of the useful arts by ensuring that patentees adequately describe their inventions in their patent specifications for the benefit of the public in exchange for the right to exclude others from practicing the invention for the duration of the patent's term.⁸

II. Evaluate Whether The Application Complies With the "Written Description" Requirement

The inquiry into whether the description requirement is met must be determined on a case-by-case basis and is a question of fact.⁹ The examiner has the initial burden of presenting evidence or reasons why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims.¹⁰ Office personnel should adhere to the following procedures when reviewing patent applications for compliance with the written description requirement of 35 U.S.C. 112, § 1.

A. Review the Entire Application To Determine What Applicant has Invented, the Field of the Invention and the Level of Predictability in the Art

Prior to determining whether the claims satisfy the written description requirement, Office personnel should review the entire specification, including the specific embodiments, figures, sequence listings, and the claims, to understand what applicant has invented and the correspondence between what applicant has described, i.e., has possession of, and what applicant is claiming. Such a review should be conducted from the standpoint of one of skill in the art at the time the application was filed and should include a determination of the field of the invention and, thus, the level of predictability in the art. Predictability of the structure of a species can be premised upon:

(1) Whether the level of skill in the art leads to a predictability of structure; and/or

(2) Whether teachings in the application or prior art lead to a predictability of structure.

There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function. Thus, in some factual situations, the written description requirement may be satisfied through disclosure of function alone when there is a well-established correlation between structure and function. In contrast, without such a correlation, prediction of structure from function is highly unlikely. In this latter case, disclosure of function alone will not

satisfy the written description requirement.¹¹

B. For Each Claim, Determine What the Claim as a Whole Covers

Each claim must be separately analyzed and given its broadest reasonable interpretation.¹² The entire claim, including its preamble language and transitional phrase, must be considered. "Preamble language" is that language in a claim appearing before a transitional phrase, e.g., before "comprising," "consisting essentially of," or "consisting of". The transitional term "comprising" (and other comparable terms, e.g., "containing" and "including") is "open-ended"—it covers the expressly recited subject matter alone or in combination with other unstated subject matter.¹³ There must be adequate written description to support the claimed invention *including* the preamble.¹⁴ The claim as a whole, including all limitations found in the preamble, the transitional phrase, and the body of the claim, must be described sufficiently to satisfy the written description requirement.¹⁵ For claims of the form "A [structure] comprising SEQ ID NO: 1" there may be a written description problem if the claim as a whole, including its preamble and transitional phrase, is directed to an invention of unpredictable structure that is not fully described.

For example, when the term "gene," "mRNA," or "cDNA" is recited in the preamble, it implies a specific structure (or a small genus of specific structures) when used in the traditional sense, i.e., to mean the structure having the naturally occurring sequence. Thus, "A gene comprising SEQ ID NO: 1"; "A mRNA comprising SEQ ID NO: 1"; and "A cDNA comprising SEQ ID NO: 1" implicitly recite specific structures such as promoters, enhancers, coding regions, and other regulatory elements in the preamble which must be sufficiently described in the specification so as to show the applicant was in possession of the claimed inventions.

In contrast, use of less specific, generic preamble language, such as "composition," "nucleic acid," "DNA," and "RNA," does not typically present a written description problem. These terms are sufficiently general that one skilled in the art can readily envision a sufficient number of members of the claimed genus to provide written description support for the genus.

A claim such as "A gene comprising SEQ ID NO: 1," can be viewed as a species claim in which the preamble recites a combination and the body of the claim recites a subcombination. The "gene" is the combination and "SEQ ID

NO: 1" (which is a fragment of the gene) is the subcombination. Written description of only the subcombination (in this example the fragment SEQ ID NO: 1) normally does not put one in possession of the combination (in this example the gene).

Likewise, generic claims to sequences can be viewed as a genus of such combination-subcombination claims. For example, a claim such as "A nucleic acid comprising SEQ ID NO: 1" can be viewed as a genus claim in which each member of the genus (each species) is itself a combination-subcombination: Each member of the genus "nucleic acid" is a combination containing the subcombination "SEQ ID NO: 1" (which is a fragment of the nucleic acid). Again, the generic term "nucleic acid" does not typically present a written description problem because one skilled in the art can readily envision a sufficient number of members of the claimed genus to provide written description support for the genus.¹⁶

C. For Each Claimed Species, Determine Whether There is Sufficient Written Description To Inform a Skilled Artisan That Applicant was in Possession of the Claimed Invention at the Time the Application was Filed

Written description may be satisfied through disclosure of relevant identifying characteristics, i.e., structure, other physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is well known to one skilled in the art need not be disclosed. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.

For each claimed species:

(1) Determine whether a complete structure is disclosed. The complete structure of a species typically satisfies the requirement that the description be set forth in "such full, clear, concise and exact terms" to show possession of the claimed invention. If a complete structure is disclosed, the written description requirement is satisfied for that species, and a rejection under 35 U.S.C. 112 ¶ 1 for lack of written description must not be made.

For example, consider the following claim:

A probe for use in detecting nucleic acid sequences coding for enzyme Q from the genus *Bacillus* consisting of SEQ ID NO: 16.

Considering the claim as a whole, it is a species claim covering the probe SEQ ID NO: 16. The specification discloses the complete sequence for SEQ ID NO: 16. Thus, this claim falls into the "safe harbor" described under C(1).

(2) If the complete structure is not disclosed, determine whether the specification discloses other relevant identifying characteristics, i.e., physical and/or chemical characteristics and/or functional characteristics coupled with a known or disclosed correlation between function and structure, sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. Disclosure of any combination of such identifying characteristics that would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. In such a case, a rejection for lack of written description under 35 U.S.C. 112 ¶ 1 must not be made.

For example, consider the following claim:

An isolated double-stranded DNA consisting of (1) a single-stranded DNA which has a molecular size of 2.57 Kb and is derived from golden mosaic virus, and (2) a DNA complementary to said single-stranded DNA, giving the restriction endonuclease cleavage map shown in FIG. 2(a) and having no Mbo I restriction endonuclease site.

Although the specification does not disclose the complete structure for the claimed DNA, it does disclose sufficient identifying characteristics, i.e., size, cleavage map, and source from which the DNA is derived. Thus, while this claim does not meet the C(1) criteria because the complete sequence is not disclosed, it does meet the C(2) criteria because one skilled in the art would recognize from the characteristics, e.g., size, map, source, that applicant was in possession of the claimed material at the time of filing.

The following protein claim also falls within the C(2) criteria:

An isolated alginate lyase enzyme wherein said enzyme lyses alginate in the mucous substance produced in a patient with cystic fibrosis and wherein said enzyme has the N-

terminal amino acid sequence SEQ ID No. 1, obtained from *Flavobacterium pepermentum* and has the following physicochemical properties: (1) Activity: lyses alginate to saccharides having a non-reducing end Ca-C_5 double bond and ultimately to 4-deoxy-5-ketouronic acid; (2) Molecular weight: 60,000 daltons; (3) Optimal pH: 8.0; (4) Stable pH: 6.0-8.0; (5) Optimal temperature: 70 degrees C; and (6) Substrate specificity: alginate.

In this example, the specification discloses the molecular weight, origin, activity, and specificity but does not disclose the complete structure for the claimed enzyme. Thus, this claim would not meet the C(1) criteria because the complete sequence is not disclosed. However, the claim meets the C(2) criteria because, although the complete structure is not disclosed, one skilled in the art would recognize from the disclosed physical characteristics—e.g., molecular weight, origin, activity, and specificity—that applicant was in possession of the claimed material at the time of filing.

In contrast, consider the following claim:

An isolated nucleotide sequence consisting of the sequence of the reverse transcript of a human mRNA, which mRNA encodes insulin.

The specification in this example provides the coding sequence for rat insulin but not that for human insulin. The description for the reverse transcript of human mRNA is limited to its function, encoding human insulin, and to a method for isolating the claimed sequence from its natural source. A sequence described only by a purely functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed species. In this case, even though a genetic code table would correlate a known insulin amino acid sequence with a genus of coding nucleic acids, the same table cannot predict the native, naturally occurring nucleic acid sequence of human mRNA or its corresponding cDNA. Thus, the specification in this example does not provide adequate written description, either under the C(1) or C(2) criteria.

Any claim to a species that does not meet the test described under C(1) or C(2) must be rejected as lacking adequate written description under 35 U.S.C. 112 ¶ 1.

D. For Each Claimed Genus, Determine Whether There is Sufficient Written Description to Inform a Skilled Artisan That Applicant was in Possession of the Claimed Genus at the Time the Application was Filed

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by relevant identifying characteristics, i.e., structure or other physical and/or chemical characteristics, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" requires that the species which are expressly described be representative of the entire genus. Thus, when there is substantial variation within the genus, it may require a description of the various species which reflect the variation within the genus. For example, a broadly drawn claim to a specific gene from ruminant mammals may require a representative species from cattle, buffalo, bison, goat, deer, antelope, camel, giraffe and llama.

What constitutes a "representative number" is an inverse function of the predictability of the art, as determined in IIA above. The number must be sufficient to reasonably identify the other members of genus. In an unpredictable art, adequate written description of a genus *cannot* be achieved by disclosing only one species within the genus. In fact, if the members of the genus are expected to vary widely in their identifying characteristics, such as structure and activity, written description for each member within the genus may be necessary.

Generalized descriptions alone, such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," fail to satisfy the written description requirement because they do not describe any members of the genus except by function without any known or disclosed correlation between function and structure.²⁴ If the correlation between structure and function in the art would not have been known to one skilled in the art and the specification does not describe the correlation, the written descriptive support cannot depend on that correlation.

For each claim to a genus:

(1) Determine whether a representative number of species have been described by complete structure as in C(1) above. If a representative number

have been so described, then the applicant has written description support for the claimed genus and a rejection under 112 ¶ 1 for lack of written description must not be made.

For example, consider the following claim to a genus:

An isolated DNA probe for detecting HIV-X, wherein said DNA probe hybridizes to the nucleotide sequence set forth in SEQ ID NO: 1 under the following conditions: hybridization in 7% sodium dodecyl sulfate (SDS), 0.5M NaPO₄, pH 7.0, 1mM EDTA at 50° C.; and washing with 1% SDS at 42° C.

In this case, the specification discloses the sequence of the isolated DNA molecule consisting of SEQ ID NO: 1 and discloses several sequences that hybridize to SEQ ID NO: 1. Hybridization under the stringent conditions specified here requires that the claimed nucleic acid probes be structurally similar to the complement of the nucleic acid sequence disclosed as SEQ ID NO: 1. In this case, the description as a whole is sufficient to evidence possession of the claimed genus because the genus is defined by relation to the structure of the sequence provided as SEQ ID NO: 1, and because several species are disclosed that possess the hybridization property which further defines the genus. Thus, this claim to a genus meets the D(1) criteria.

(2) For each claim to a genus not supported as described under D(1), determine whether there is a representative number of adequately described species, as analyzed under C(2). The representative number must permit one skilled in the art to reasonably identify the remaining members of the genus. If a representative number are so described, then the written description requirement is satisfied and, again, a rejection under 112 ¶ 1 for lack of written description must not be made.

For example, consider the following claim to a genus:

A monoclonal antibody which specifically binds to the novel cancer associated TAG-31 antigen but which does not substantially bind normal adult human tissues, wherein said monoclonal antibody has a binding affinity of greater than 3 times 10⁹ M⁻¹ for TAG-31.

Considering the claim as a whole, it is drawn to a genus of monoclonal antibodies. Although the specification does not disclose the complete structure of a representative number of species to support the claimed genus of antibodies, it does disclose multiple monoclonal antibodies which have the isotype claimed as well as the binding specificity and binding affinity

characteristics recited in the claims. In this well-developed art, additional identifying characteristics for a substantial portion of the genus are well-known (e.g., number of chains, disulfide bonds, constant and variable regions, etc.). Thus, applicant's disclosure combined with what was known in the art are sufficient to describe the claimed genus of monoclonal antibodies in such full, clear, concise and exact terms to show applicant was in possession of the claimed antibodies. Thus, the claim meets the D(2) criteria.

As another example, consider the following claim to a genus:

An isolated mutanase enzyme produced by *Bacillus* having the following physicochemical properties (1) to (9): (1) action: an ability to cleave alpha-1,3-glucosidic links of mutan; (2) substrate specificity: an ability to effectively decompose mutan; (3) optimum pH: pH 4 to 4.5 when reacting on a mutan substrate at 35 degrees C for 10 minutes; (4) pH range for stability: pH 4 to 10 when kept at 25 degrees C for 24 hours; (5) optimum temperature: 50 degrees to 65 degrees C when reacted at pH 5 with mutan as a substrate; (6) thermal stability: enzyme activity remains stable below 50 degrees C after incubation at pH 5 for 10 minutes; (7) effect of metal ions: mercury and silver show inhibitory effect on a mutan substrate; (8) effect of inhibitors: p-chloromercuribenzoic acid shows inhibitory effect on a mutan substrate; and (9) molecular weight: about 140,000 to about 160,000 as determined by SDS-polyacrylamide gel electrophoresis.

Considering the claim as a whole, it covers a genus of mutanase enzymes. Although the specification does not disclose the complete structure of a representative number of species to support the claimed genus of enzyme compositions, it does disclose 3 mutanase species produced by different strains of *Bacillus* (mutanases A, B and C) which are identified by multiple relevant identifying characteristics, i.e., molecular weight, substrate specificity, optimum and ranges of temperature and pH for mutan cleavage activity, etc. In this well-developed art, these identifying characteristics are sufficient for a skilled artisan to recognize applicant had possession of the species from the identifying characteristics of the three mutanase species, to reasonably predict sufficient identifying characteristics of the other members of the genus and, thus, establish possession of the genus. Thus, the claim meets the D(2) criteria.

As another example, consider the following claim to a genus:

A DNA comprising a novel DF3 enhancer and DNA encoding a heterologous gene but not encoding DF3 wherein said DF3 enhancer consists of SEQ ID NO: 1.

Considering the claim as a whole, it covers a genus of DNA. The specification does not describe a representative number of members of the genus by complete structure. Thus, the claim does not meet the D(1) criteria. However, there is sufficient disclosure of identifying characteristics common to the members of the genus, i.e., DF3 enhancer, to meet the D(2) criteria. Because of the nature of the generic term "DNA," one skilled in the art could envision a sufficient number of the members of the genus to describe the invention in such full, clear and concise terms as to show possession of the invention at the time of filing.

In contrast, consider the claim:

An isolated nucleic acid comprising the structure of the reverse transcript of a mammalian mRNA, which mRNA encodes insulin.

Considering the claim as a whole, the claim covers the genus of nucleotide sequences encoding mammalian insulin. The specification only provides the coding sequence for rat insulin cDNA and a method to isolate the coding sequence from its natural source.²⁵ This description does not meet the criteria of D(1) or D(2) and thus does not satisfy the written description requirement.

Also contrast the claim "A gene comprising SEQ ID NO: 1." Although all genes encompassed by this claim share the characteristic of comprising SEQ ID NO: 1, and as such might appear to meet the D(2) criteria, there is insufficient description of the characteristics (e.g., promoters, enhancers, coding regions, and other regulatory elements) which identify the genes, as opposed to any DNA comprising SEQ ID NO: 1.

If sufficient identifying characteristics are not disclosed for a given genus, as described in D(1) or D(2), the claim to that genus must be rejected as lacking adequate written description under 35 U.S.C. 112 ¶ 1.

III. Complete Patentability Determination Under All Statutory Requirements and Clearly Communicate Findings, Conclusions and Their Bases

The above only describes how to determine whether the written description requirement of 35 U.S.C. 112 ¶ 1 is satisfied. Regardless of the outcome of that determination, Office personnel must complete the patentability determination under all the relevant statutory provisions of the Patent Act.

Once Office personnel have concluded analysis of the claimed invention under all the statutory provisions, including 35 U.S.C. 101, 112, 102 and 103, they should review all the proposed rejections and their bases to confirm their correctness. Only then should any rejection be imposed in an Office action. The Office action should clearly communicate the findings, conclusions and reasons which support them.

Specific to these guidelines:

A. For Each Claim Lacking Written Description Support, Reject the Claim Under Section 112, ¶ 1, for Lack of Adequate Written Description

In rejecting a claim, set forth express findings of fact regarding the above analysis which support the lack of written description conclusion. These findings should:

(1) identify the claim limitation not described; and

(2) provide reasons why a person skilled in the art at the time the application was filed would not have recognized the description of this limitation in view of the disclosure of the application as filed.

When appropriate, suggest amendments to the claims which would bring the claims into compliance with the written description in the specification, bearing in mind the prohibition against new matter in the claims and corresponding description set forth in 35 U.S.C. 112 and 132.

B. Upon Reply by Applicant, Again Determine the Patentability of the Claimed Invention, Including Whether the Written Description Requirement is Satisfied by Performing the Analysis Described Above in View of the Whole Record

Upon reply by applicant, before repeating any rejection under Section 112 ¶ 1 for lack of written descriptive basis, review the basis for the rejection in view of the record as a whole, including amendments, arguments and any evidence submitted by applicant. If the whole record now demonstrates that the written description requirement is satisfied, do not repeat the rejection in the next Office action. If the record still does not demonstrate that written description is adequate to support the claim(s), repeat the rejection under 35 U.S.C. 112 ¶ 1, fully respond to applicant's rebuttal arguments, and properly treat any further showings submitted by applicant in the reply. Any affidavits, including those relevant to the 112 ¶ 1 written description requirement, must be thoroughly

analyzed and discussed in the Office action.

Endnotes

1. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

2. 984 F.2d 1164, 25 USPQ2d 1601 (Fed. Cir. 1993).

3. 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991).

4. E.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991).

5. *In re Barker*, 559 F.2d 588, 592 n.4, 194 USPQ 470, 473 n.4 (CCPA 1977).

6. 35 U.S.C. §§ 132 & 251.

7. E.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Much of the written description case law addresses whether the specification as originally filed supports claims not originally in the application. The issue raised in the cases is most often phrased as whether the original application provides "adequate support" for the claims at issue or whether the material added to the specification incorporates "new matter" in violation of 35 U.S.C. § 132. The "written description" question similarly arises in the interference context, where the issue is whether the specification of one party to the interference can support the newly added claims corresponding to the count at issue, i.e., whether that party can "make the claim" corresponding to the interference count. E.g., see *Martin v. Mayer*, 823 F.2d 500, 502, 3 USPQ2d 1333, 1335 (Fed. Cir. 1987).

In addition, early opinions suggest the Patent and Trademark Office was unwilling to find written descriptive support when the only description was found in the claims; however, this viewpoint was rejected. See *In re Koller*, 613 F.2d 819, 204 USPQ 702 (CCPA 1980) (original claims constitute their own description); *In re Gardner*, 475 F.2d 1389, 177 USPQ 396 (CCPA 1973) (accord); *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976) (accord). It is now well-accepted that a satisfactory description can be mined from the claims or any other portion of the originally filed specification.

These early opinions did not address the quality or specificity of particularity that was required in the description, i.e., how much description is enough.

8. See *Eli Lilly*, 119 F.3d at 1566, 43 USPQ2d at 1404.

9. See *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) ("Precisely how close [to the claimed invention] the description must come to comply with § 112 must be left to a case-by-case development."); *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976) (inquiry is primarily factual and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure).

10. *Wertheim*, 541 F.2d at 262, 191 USPQ at 96.

11. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 (written description requirement not satisfied by merely providing "a result that one might achieve if one made that invention"); *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73

(Fed. Cir. 1984) (affirming a rejection for lack of written description because the specification does "little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate").

12. See, e.g., *In re Morris*, 127 F.3d 1048, 1053-54, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997).

13. See, e.g., *Ex parte Davis*, 80 USPQ 448, 450 (1948) ("comprising" leaves the "claim open for the inclusion of unspecified ingredients even in major amounts"), quoted with approval in *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 1271, 229 USPQ 805, 812 (Fed. Cir. 1986).

14. See *Pac-Tec Inc. v. Amerace Corp.*, 903 F.2d 796, 801, 14 USPQ2d 1871, 1876 (Fed. Cir. 1990) (determining that preamble language that constitutes a structural limitation is actually part of the claimed invention).

15. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

16. E.g., *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1405-06.

17. A "relevant identifying characteristic" is one that would provide evidence that applicant was in possession of what is claimed. For example, the presence of a restriction enzyme map of a gene may be relevant to a statement that the gene has been

isolated. One skilled in the art could determine whether the gene disclosed was the same as or different than a gene isolated by another by comparing the restriction enzyme map. In contrast, evidence that the gene could be digested with a nuclease would not normally represent a relevant characteristic since any gene would be digested with a nuclease.

Examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics can demonstrate the requisite possession. For example, unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross reactivity may be sufficient to show possession of the claimed invention to one of skill in the art. See *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997) ("written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams, formulas, etc. that fully set forth the claimed invention").

However, a definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. See also *Fiers*, 984 F.2d at

1169-71, 25 USPQ2d at 1605-06 (discussing Amgen).

18. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986).

19. See, e.g., *Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in *ipsis verbis* to be sufficient").

20. 35 U.S.C. § 112 ¶ 1. *Cf. Fields v. Conover*, 443 F.2d 1386, 1392, 170 USPQ 276, 280 (CCPA 1971) (finding a lack of written description because the specification lacked the "full, clear, concise, and exact written description" which is necessary to support the claimed invention).

21. The examples contained within these guidelines are not intended to represent the minimum requirements necessary to comply with 35 U.S.C. § 112 ¶ 1.

22. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

23. See *id.* at 1568, 43 USPQ2d at 1406.

24. *Cf. Eli Lilly*, 119 F.3d at 1567, 43 USPQ2d at 1405 (stating that "The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning itself").

25. See *id.* 1568, 43 USPQ2d at 1406.

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